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Proposed Re-evaluation Decision

Imazamethabenz-Methyl

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Overview

Proposed Re-evaluation Decision for Imazamethabenz-methyl

After a thorough re-evaluation of the herbicide imazamethabenz-methyl, Health Canada's Pest Management Regulatory Agency (PMRA), under the authority of the *Pest Control Products Act* is proposing continued registration of products containing imazamethabenz-methyl for sale and use in Canada.

An evaluation of available scientific information found that products containing imazamethabenz-methyl have value in the food and crop industry and do not present unacceptable risks to human health or the environment. As a condition of the continued registration of imazamethabenz-methyl use on various food, feed, industrial oilseed and fibre crops including spring and durum wheat, sunflower, spring barley and annual ryegrass grown only for seed, new risk reduction measures are proposed for the labels of all products. No additional data are being requested at this time.

The PMRA's pesticide re-evaluation program considers potential risks as well as the value of pesticide products to ensure they meet modern standards established to protect human health and the environment. Regulatory Directive DIR2001-03, *PMRA Re-evaluation Program*, presents the details of the re-evaluation activities and program structure. Re-evaluation draws on data from registrants, published scientific reports, information from other regulatory agencies and any other relevant information available.

This proposal affects all end-use products containing imazamethabenz-methyl registered in Canada. Once the final re-evaluation decision is made, registrants will be instructed on how to address any new requirements.

This Proposed Re-evaluation Decision is a consultation document[1] that summarizes the science evaluation for imazamethabenz-methyl and presents the reasons for the proposed re-evaluation decision. It also proposes additional risk-reduction measures to further protect human health and the environment.

The information is presented in two parts. The Overview describes the regulatory process and key points of the evaluation, while the Science Evaluation provides detailed technical information on the human health, environmental and value assessment of imazamethabenz-methyl.

The PMRA will accept written comments on this proposal up to 60 days from the date of publication of this document. Please forward all comments to Publications (please see contact information on the cover page of this document).

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1 "Consultation statement" as required by subsection 28(2) of the *Pest Control Products Act*.

What Does Health Canada Consider When Making a Re-evaluation Decision?

The key objective of the *Pest Control Products Act* is to prevent unacceptable risks to people and the environment from the use of pest control products. Health or environmental risk is considered acceptable if there is reasonable certainty that no harm to human health, future generations or the environment will result from use or exposure to the product under its conditions or proposed conditions of registration.[2] The Act also requires that products have value[3] when used according to the label directions. Conditions of registration may include special precautionary measures on the product label to further reduce risk.

To reach its decisions, the PMRA applies hazard and risk assessment methods as well as policies that are rigorous and modern. These methods consider the unique characteristics of sensitive subpopulations in both humans (e.g. children) and organisms in the environment (e.g. those most sensitive to environmental contaminants). These methods and policies also consider the nature of the effects observed and the uncertainties present when predicting the impact of pesticides. For more information on how the PMRA regulates pesticides, the assessment process and risk-reduction programs, please visit the PMRA's website at www.pmra-arla.gc.ca.

Before making a re-evaluation decision on imazamethabenz-methyl, the PMRA will consider all comments received from the public in response to this consultation document[4]. The PMRA will then publish a Re-evaluation Decision[5] on imazamethabenz-methyl, which will include the decision, the reasons for it, a summary of comments received on the proposed registration decision and the PMRA's response to these comments.

For more details on the information presented in this overview, please refer to the Science Evaluation section of this consultation document.

What Is Imazamethabenz-Methyl?

Imazamethabenz-methyl is a selective systemic herbicide registered for postemergent use on wheat (spring and durum) and spring barley. It is registered for use in the Prairie provinces and the Peace River region, the Okanagan Valley and the Creston Flats areas of British Columbia on sunflower and annual ryegrass grown only for seed in the Prairie provinces. Imazamethabenz-methyl can also be used to control wild oats and broadleaf weeds including wild mustard, stinkweed, wild buckwheat and tartary buckwheat. It is applied once per year at a rate of 250 to 500 g a.i./ha by ground equipment only.

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2 "Acceptable risks" as defined by subsection 2(2) of the *Pest Control Products Act*.

3 "Value" as defined by subsection 2(1) of the *Pest Control Products Act*: "the product's actual or potential contribution to pest management, taking into account its conditions or proposed conditions of registration, and includes the product's (a) efficacy; (b) effect on host organisms in connection with which it is intended to be used; and (c) health, safety and environmental benefits and social and economic impact."

4 "Consultation statement" as required by subsection 28(2) of the *Pest Control Products Act*.

5 "Decision statement" as required by subsection 28(5) of the *Pest Control Products Act*.

Health Considerations

Can Approved Uses of Imazamethabenz-Methyl Affect Human Health?

Imazamethabenz-methyl is unlikely to affect your health when used according to the revised label directions.

Potential exposure to imazamethabenz-methyl may occur through diet (food and water), when handling and applying the product or by prematurely entering treated sites. When assessing health risks, two key factors are considered: the levels at which health effects occur in animal testing and the levels to which people may be exposed. The dose levels used to assess risks are established to protect the most sensitive human population (e.g. children and nursing mothers). Only uses for which the exposure is well below levels that cause no effects in animal testing are considered acceptable for registration.

Toxicology studies in laboratory animals describe potential health effects from varying levels of exposure to a chemical and identify the dose where no effects are observed. The health effects noted in animals occur at doses more than 100-times higher (and often much higher) than levels to which humans are normally exposed when imazamethabenz-methyl products are used according to label directions.

Imazamethabenz-methyl was slightly irritating to the eyes, but was not an irritant to the skin of rabbits nor was it a sensitizer in guinea pigs. Consequently, no hazard statements are required on the label of the technical class product.

Imazamethabenz-methyl did not cause cancer in animals, was not genotoxic or teratogenic and showed no signs of neurotoxicity. The liver was the main target of toxicity in rats. The first signs of toxicity in dogs given daily doses of imazamethabenz-methyl over longer periods of time were slight changes in hematology along with effects on organ weights and decreased body weight. In mice, effects on organ weights were also noted at high doses.

When imazamethabenz-methyl was given to pregnant animals, effects on the developing fetus were observed at doses that were toxic to the mother, indicating that the fetus is not more sensitive to imazamethabenz-methyl than the adult animal. The risk assessment protects against these effects by ensuring that the level of human exposure is well below the lowest dose at which these effects occurred in animal tests.

Residues in Water and Food

Dietary risks from food and water are not of concern.

Reference doses define levels to which an individual can be exposed over a single day (acute) or lifetime (chronic) and expect no adverse health effects. Generally, dietary exposure from food and water is acceptable if it is less than 100% of the acute reference dose or chronic reference dose (acceptable daily intake). An acceptable daily intake (ADI) is an estimate of the level of daily exposure to a pesticide residue that, over a lifetime, is believed to have no significant harmful effects.

Human exposure to imazamethabenz-methyl was estimated from residues in treated crops and drinking water, including the most highly exposed subpopulation (e.g. children one to six years old). Conservative assumptions were used to reflect the magnitude of the residues as well as the percent crop treated. As well, information on drinking water was used to estimate both the acute and chronic aggregate exposures and risks.

Only long term (chronic) exposure estimates were determined for different subpopulations representing different ages, genders and reproductive status. Acute and cancer dietary assessments were not required.

Aggregate chronic exposure (i.e. to imazamethabenz-methyl from food and drinking water) represents 6% and 23% of the chronic reference dose for the general population and non-nursing infants, respectively, when using drinking water modelling. As a result, chronic risks were below the PMRA's level of concern.

The *Food and Drugs Act* prohibits the sale of adulterated food, that is, food containing a pesticide residue that exceeds the established maximum residue limit (MRL). Pesticide MRLs are established for *Food and Drugs Act* purposes through the evaluation of scientific data under the *Pest Control Products Act.* Each MRL value defines the maximum concentration in parts per million (ppm) of a pesticide allowed in or on certain foods. Food containing a pesticide residue that does not exceed the established MRL does not pose an unacceptable health risk.

MRLs for imazamethabenz-methyl are currently specified for barley, sunflower and wheat. No modification of the MRLs was proposed during the course of the re-evaluation. Where no specific MRL has been established, a default MRL of 0.1 ppm applies, which means that pesticide residues in a food commodity must not exceed 0.1 ppm. MRLs for imazamethabenz-methyl can be found in the Science Evaluation, Table 8.1.1.3, of this consultation document.

Risks in Residential and Other Non-Occupational Environments

Residential and other non-occupational risks are not of concern.

Imazamethabenz-methyl is not registered for use in any residential areas. Therefore, a non-occupational risk assessment was not required.

Occupational Risks From Handling Imazamethabenz-Methyl

Occupational risks are not of concern when used according to the revised label directions.

Based on the precautions and directions for use on the original product labels reviewed for this re-evaluation and considering the use of appropriate protective equipment, the risk estimates associated with mixing, loading and applying activities meet current standards for all the scenarios and are not of concern. The proposed personal protective equipment are long pants, a long-sleeved shirt, shoes plus socks and chemical-resistant gloves.

Postapplication risks are not of concern when used according to the revised label directions.

Occupational postapplication risk assessments consider exposures of workers entering treated agricultural sites. Based on the precautions and directions for use on the original product labels reviewed for this re-evaluation and considering the proposed protective measures (revised restricted-entry interval), postapplication risk estimates to re-entry workers performing scouting activities meet current standards and are not of concern.

Environmental Considerations

What Happens When Imazamethabenz-Methyl Is Introduced Into the Environment?

Imazamethabenz-methyl poses a potential risk to terrestrial and aquatic plants, therefore, additional risk reduction measures need to be observed

When imazamethabenz-methyl is applied to control weeds in crops, some of it finds its way into soil and water. The chemical is expected to be slightly persistent to persistent in soil as it is degraded by soil microbes. It is non-persistent to moderately persistent in alkaline and acidic water, respectively. Both imazamethabenz-methyl and its breakdown product, imazamethabenz-methyl acid, are mobile and hence can move freely in soil. The high solubility, the leaching studies and the results of the adsorption/desorption studies indicate that imazamethabenz-methyl and imazamethabenz-methyl acid have the potential to reach groundwater. However, field evidence indicates that imazamethabenz-methyl alone remains within the top 15 cm of the soil after application. Water monitoring of ponds and rivers have revealed residues from runoff but at concentrations below levels of concern for aquatic life. Several major transformation products from the breakdown of

imazamethabenz-methyl would be present in soil and aquatic systems, but their fate in the environment, especially that of imazamethabenz-methyl acid, have not been fully characterized.

When imazamethabenz-methyl is used for weed control in crops, there is a potential that sensitive plant species on land and in water may be exposed to the chemical as a result of the spray drift and runoff. Some of these species are sensitive to the chemical and would be adversely affected. To reduce effects in non-target areas, spray buffer zones between the agricultural field and the non-target terrestrial or aquatic areas is proposed. The width of these buffer zones will be specified on the product label. Imazamethabenz-methyl presents negligible risk to wild birds, mammals, bees, earthworms, fish, amphibians, aquatic invertebrates and algae because concentrations in the environments are expected to be at levels that are not harmful.

Value Considerations

What Is the Value of Imazamethabenz-Methyl?

Imazamethabenz-methyl controls wild oats and some broadleaf weeds in several crops.

In Western Canada, imazamethabenz-methyl reduces a portion of the estimated $343.9 million in economic losses incurred by weeds for barley, wheat and sunflower. It is one of two herbicides used for the control of wild mustard and stinkweed in sunflower and annual ryegrass grown only for seed. Imazamethabenz-methyl can be tank-mixed with other herbicides to broaden the spectrum of weed control. Although populations of imazamethabenz-methyl-resistant wild oats have been identified in Canada, imazamethabenz-methyl can readily be used in locations lacking resistant populations in rotation with other herbicide groups including Groups 1, 3, 8, 9, 10, 11 or 16 to mitigate resistance development in populations of wild oats. Being a Group 2 herbicide imazamethabenz-methyl plays a role in managing resistance development to other herbicide groups.

Measures to Minimize Risk

Registered pesticide product labels include specific instructions for use. Directions include risk-reduction measures to protect human and environmental health. These directions must be followed by law .

Risk-reduction measures are being proposed to address potential risks identified in this assessment. These measures, in addition to those already identified on existing imazamethabenz-methyl product labels, are designed to further protect human health and the environment. The following additional key risk-reduction measures are being proposed.

Additional Key Risk-Reduction Measures

Human Health

- Mixers, loaders and applicators must wear a long-sleeved shirt, long pants, shoes plus socks and chemical-resistant gloves. Gloves not required for groundboom sprayers.
- Workers must not re-enter treated fields until 12 hours after application.
- Application must only occur when the potential for drift to areas of human habitation or activity (i.e. houses, cottages, schools and recreational areas) is minimal. Applicators must take into consideration wind speed, wind direction, temperature, the application equipment used and sprayer settings.

Environment

- Updated precautionary statements and terrestrial and aquatic buffer zones (0 to 1 m) are required to protect terrestrial and aquatic habitats that may contain sensitive plant species.

Next Steps

Before making a re-evaluation decision on imazamethabenz-methyl, the PMRA will consider all comments received from the public in response to this consultation document. The PMRA will then publish a Re-evaluation Decision, which will include the decision, the reasons for it, a summary of comments received on the proposed decision and the PMRA's response to these comments.

Other Information

When the re-evaluation decision is made, the PMRA will publish an Evaluation Report on imazamethabenz-methyl in the context of this re-evaluation decision (based on the Science Evaluation section of this consultation document). In addition, the test data on which the decision is based will also be available for public inspection, upon application, in the PMRA's Reading Room (located in Ottawa).

Science Evaluation

1.0 Introduction

Imazamethabenz-methyl is a selective systemic herbicide. It belongs to the imidazolinone chemical family and is classified as a Group 2 herbicide. The herbicidal activity of imazamethabenz-methyl inhibits the plant enzyme acetolactate synthase (ALS), also called acetohydroxyacid synthase.

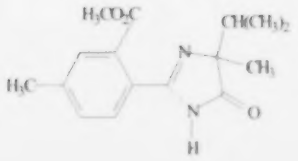
Following the re-evaluation announcement for imazamethabenz-methyl, Nufarm Agriculture Inc., the sole registrant of the technical grade active ingredient and primary data provider in Canada, indicated it would continue to support all uses included on the label of Commercial Class end-use products. There are no Domestic Class products containing imazamethabenz-methyl registered in Canada.

2.0 The Technical Grade Active Ingredient, Its Properties and Uses

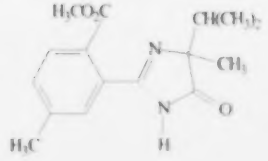
2.1 Identity of the Technical Grade Active Ingredient

Common name		Imazamethabenz-methyl
Function		Herbicide
Chemical family		Imidazolinone
Chemical name		
1.	**International Union of Pure and Applied Chemistry (IUPAC)**	meta: methyl (±)-6-(4-isopropyl-4-methyl-5-oxo-2-imidazolin-2-yl)-m-toluate para: methyl (±)-2-(4-isopropyl-4-methyl-5-oxo-2-imidazolin-2-yl)-p-toluate
2.	**Chemical Abstracts Service (CAS)**	meta: methyl (±)-2-[4,5-dihydro-4-methyl-4-(1-methylethyl)-5-oxo-1H-imidazol-2-yl]-5-methylbenzoate para: methyl (±) 2-[4,5-dihydro-4-methyl-4-(1-methylethyl)-5-oxo-1H-imidazol-2-yl]-4-methylbenzoate
CAS registry number		81405-85-8
Molecular formula		$C_{16}H_{20}N_2O_3$
Molecular weight		288.35 amu

Structural formula



Meta



Para

Based on the manufacturing process used, impurities of human health or environmental concern as identified in the *Canada Gazette*, Part II, Vol. 139, No. 24, SI/2005-114 (2005-11-30), including Toxic Substances Management Policy (TSMP) Track 1 substances, are not expected to be present in the product.

2.2 Physical and Chemical Properties of the Technical Grade Active Ingredient

Property	Result
Vapour pressure at 25°C	1.5×10^{-3} mPa
Ultraviolet (UV)/visible spectrum	Not expected to absorb at λ>250 nm
Solubility in water	1370 (*m*-isomer)mg/kg 857 (*p*-isomer)mg/kg
n-Octanol–water partition coefficient	log K_{ow} = 1.54 *p*-isomer log K_{ow} = 1.82 *m*-isomer
Dissociation constant	pKa = 2.9 at 23.5°C

2.3 Description of Registered Imazamethabenz-Methyl Uses

Appendix I lists all imazamethabenz-methyl products registered under the authority of the *Pest Control Products Act*, specifically one technical grade active ingredient and three Commercial Class end-use products.

Appendix II lists all the uses for which imazamethabenz-methyl is presently registered. All uses were supported by the registrant at the time of re-evaluation and were, therefore, considered in the health and environmental risk assessments.

Uses of imazamethabenz-methyl belong to the following use-site categories: industrial oil seed crops and fibre crops, terrestrial feed crops, and terrestrial food crops. Theses crop uses include sunflower, wheat (spring and durum), spring barley, and annual ryegrass grown only for seed.

3.0 Impact on Human and Animal Health

Toxicology studies in laboratory animals describe the potential health effects resulting from various levels of exposure to a chemical and identify dose levels where no effects are observed. Unless there is evidence to the contrary, it is assumed that effects observed in animals are relevant to humans and that humans are more sensitive to effects of a chemical than the most sensitive animal species. The health effects noted here were observed in animals at dose levels at least 100-fold (often much higher) above levels to which humans are normally exposed through use of products containing this chemical.

3.1 Toxicological Summary

A detailed review of the toxicological database for imazamethabenz-methyl was conducted. The database is complete, consisting of the full array of toxicity studies currently required for hazard assessment purposes. At that time all of these studies were conducted in accordance with the accepted international testing protocols and Good Laboratory Practices. The scientific quality of the data is high and the database is considered adequate to define the majority of the toxic effects that may result from exposure to this chemical pest control product.

Imazamethabenz-methyl technical is a mixture of 42% meta and 58% *p*-isomers with a range of 38 to 45% meta and 55 to 62% para isomers. Imazamethabenz-methyl technical's toxic action is dependent on conversion to the parent acid (CL 263,840).

In acute toxicity studies, imazamethabenz-methyl technical is of low toxicity by the oral (rats, mice), dermal (rabbits) and inhalation (rats) routes of exposure. The technical material induced slight irritation in the eyes of rabbits and was not an irritant to the skin of rabbits nor was it a sensitizer in guinea pigs. When tested alone, the para and meta isomers had low acute toxicity by the oral and dermal routes. Both the para and meta isomers were mild skin and eye irritants in rabbits. No data on inhalation or skin sensitization were available for the para- and meta-isomers alone.

When tested in rats by the oral route of exposure, the acute toxicity of the parent acid was demonstrated to be comparable to that of imazamethabenz-methyl technical. Based on the low acute toxicity of both of these compounds, the repeat-dose toxicity studies conducted in mammals with imazamethabenz-methyl technical should cover off any concern for the potential toxicity induced in animals exposed to the parent acid.

Metabolism studies in male and female rats exposed to a single oral or intravenous dose of imazamethabenz-methyl technical indicated that it is rapidly absorbed from the gastrointestinal tract. After 24 hours, the highest tissue residue levels were found in the liver, kidneys, fat, muscle and blood with residue levels being quite low seven days after dosing. It was determined that the technical material was excreted primarily in the urine (77 to 78%) with 13 to 19% of the administered radioactivity excreted in the feces. The route of dosing or treatment with low or high-dose levels did not alter the excretion profiles. The para and meta isomers are both rapidly metabolized by similar pathways and the acid form of parent material is the major metabolite. The major metabolic processes are the hydrolytic cleavage of the methyl ester linkage and the

hydroxylation of the methyl group in the benzene ring. The result is the formation of the parent acid as the major metabolite, and hydroxymethyl analog of the acid, and hydroxymethyl analogs of the parent esters as the minor metabolites. There are no apparent sex-related differences in the uptake, metabolism or excretion of the test material.

In repeat-dose dietary studies, the liver was the main target of toxicity with dose-related alterations in liver weights. At the lowest effect levels histopathology was noted in rats and dogs (but not mice). Rats exposed to imazamethabenz-methyl for two years also experienced decreased body weights and body-weight gains among both sexes. In dogs, slight hematological effects (reduced hemoglobin, red blood cells and hematocrit) along with increased relative liver, spleen and heart weights and decreased body weight were noted at the lowest effect levels. In a short-term dermal toxicity study in rabbits, mild to moderate skin irritation was noted starting at the low dose, with no evidence of systemic toxicity. Repeat-dose inhalation studies were not available. No clear gender sensitivities were seen in short-term or chronic repeat-dose toxicity studies. There is limited evidence of increased toxicity with increased duration of exposure in rats, based on the adverse effects on body weight at lower doses in longer-term studies.

Imazamethabenz-methyl was considered non-mutagenic based on negative results obtained from an in vivo dominant lethal study on rats and in in vitro assays including a chromosomal aberration study in Chinese hamster ovary (CHO) cells, unscheduled DNA synthesis in rat hepatocytes, a point mutation test in eukaryotic cells and in an Ames assay with *Salmonella typhimurium*.

Imazamethabenz-methyl did not show evidence of carcinogenicity in the chronic studies conducted with mice or rats. In an 18 month chronic/oncogenicity mouse study conducted by the oral route, increases in relative thyroid, parathyroid and adrenal weights were noted at study termination in high-dose males and in mid- and high-dose females.

A developmental toxicity study conducted by gavage in rats revealed no significant treatment related signs of maternal toxicity. An increased incidence of total malformations was noted at the limit dose in the absence of statistical significance (one fetus with thread-like tail, anal atresia and absence of all caudal vertebrae; one fetus with cleft palate with short lower jaw). The incidence of anal atresia was within the historical control values and the presence of the thread-like tail and absence of all caudal vertebrae was likely associated with the anal atresia. The presence of cleft palate, occurring in one high-dose fetus also displaying short lower jaw, was also within the historical control data. Three additional fetuses at the limit dose displayed delayed ossification of the caudal vertebra but, this was not considered treatment-related in the absence of other ossification delays. Based on the absence of significant maternal or fetal effects, there is no evidence of teratogenicity or developmental toxicity in the rat. A gavage developmental toxicity study conducted with slightly lower doses in the rabbit resulted in no treatment-related teratogenic effects. Effects noted in the dams included decreased body-weight gain. An increased number of postimplantation losses per gravid dam was noted at maternally toxic doses.

In a three-generation rat reproduction study, slightly decreased body weight and body-weight gain were noted in the dams. There were also no signs of treatment-related toxicity on reproductive parameters or in the offspring.

Results of the acute and chronic tests conducted on laboratory animals with the technical class product, along with the toxicology endpoints for use in the human health risk assessment, are summarized in Appendix III and Appendix IV.

***Pest Control Products Act* Hazard Characterization**

For assessing risks from potential residues in food or from products used in or around homes or schools, the *Pest Control Products Act* requires the application of an additional 10-fold factor to threshold effects. This factor should take into account the completeness of the data with respect to the exposure of, and toxicity to, infants and children and potential prenatal and postnatal toxicity. A different factor may be determined to be appropriate based on reliable scientific data.

With respect to the completeness of the toxicity database as it pertains to the exposure of and toxicity to infants and children, extensive data were available for imazamethabenz-methyl. Data of high quality was available for imazamethabenz-methyl and included one developmental toxicity study in rats, one developmental toxicity study in rabbits and a multigeneration reproduction study in rats.

With respect to potential prenatal and postnatal toxicity, the pre-natal developmental toxicity studies in rats and rabbits provided no indication of increased susceptibility of fetuses to in utero exposure. An increased postimplantation loss was noted in pregnant rabbits, but only at a dose causing maternal toxicity (decreased body-weight gain). In the rat reproduction study there was no indication of increased susceptibility in the offspring compared to parental animals. There is a low level of concern for potential prenatal and postnatal toxicity associated with imazamethabenz-methyl.

3.2 Occupational and Non-Occupational Risk Assessment

Occupational and non-occupational risks are estimated by comparing potential exposures with the most relevant endpoint from toxicology studies to calculate a margin of exposure (MOE). This is compared to a target MOE incorporating uncertainty factors protective of the most sensitive subpopulation. If the calculated MOE is less than the target MOE, it does not necessarily mean that exposure will result in adverse effects. However, MOEs less than the target MOE require measures to mitigate (reduce) risk.

3.2.1 Toxicological Endpoints

Short- and Intermediate-term Dermal Risk Assessment

For occupational short-term (1–30 days) and intermediate-term (1 month to several months) dermal assessments relative to the use pattern, the no observed adverse effect level (NOAEL) of 200 mg/kg bw/day from the 21-day dermal toxicity study with New Zealand White rabbits was selected. No treatment related signs of systemic toxicity were observed at any of the dose levels studied. The target MOE selected when using this study is 100, thus accounting for standard

uncertainty factors of 10-fold for interspecies extrapolation and 10-fold for intraspecies variability. The selection of this study and MOE is considered to be protective of all populations including nursing infants and the unborn children of exposed female workers.

Short- and Intermediate-term Inhalation Risk Assessment
Given there are no repeat-dose inhalation studies available for inhalation risk exposure, it is appropriate to assume that absorption via inhalation exposure is equivalent to oral absorption.

For occupational short-term (1 to 30 days) and intermediate-term (1 month to several months) inhalation assessment relative to the use pattern, the NOAEL of 25 mg/kg bw/day from the 1 year dietary toxicity study with dogs was selected. At the next dose level of 100 mg/kg bw/day, increased relative spleen, heart and liver weights, decreased body weights and slight hematological effects (reduced hemoglobin, red blood cells and hematocrit) were noted in males with females experiencing the slight hematological effects. The target MOE selected when using this study is 100, thus accounting for standard uncertainty factors of 10-fold for interspecies extrapolation and 10-fold for intraspecies variability. This target MOE is protective of the postimplantation losses observed in rabbits at higher dose levels of imazamethabenz-methyl and is considered protective of all populations, including pregnant women, infants and children.

Dermal Absorption
A NOAEL from a suitable dermal study was available for use in the dermal risk assessment. Therefore, a dermal absorption value is not required.

3.2.2 Occupational Exposure and Risk Assessment

Workers can be exposed to imazamethabenz-methyl through mixing, loading or applying the herbicide during normal use and when re-entering a treated site to conduct activities such as scouting and/or handling treated crops.

3.2.2.1 Mixer/Loader/Applicator Exposure and Risk

There are potential exposures to mixers, loaders and applicators. The following supported uses were assessed:

- mixing and loading the emulsifiable concentrate for application to field crops;
- mixing and loading the suspension for application to field crops;
- mixing and loading the soluble granules for application to field crops; and
- applying the liquids as sprays to field crops by groundboom sprayer.

Occupational handlers of imazamethabenz-methyl include farmers and custom agricultural applicators who mix, load and apply the herbicide. As only one application is permitted per year, the duration of exposure for farmers is expected to be short-term (up to 30 days). In the case of custom applicators, the duration of exposure may be intermediate (1 to 6 months). Exposure for all crop scenarios is predominantly dermal, with inhalation accounting for a minor component of overall exposure.

The PMRA estimated handler exposure based on the following level of personal protective equipment (PPE):

Baseline PPE:	Long pants, a long-sleeved shirt, shoes plus socks and chemical-resistant gloves unless specified otherwise (i.e. for groundboom application, chemical-resistant gloves are not included in the scenario)

Mixer/loader/applicator exposure estimates are based on the best available data at this time. The assessment might be refined using product-specific exposure data or biological monitoring data.

No chemical specific exposure studies were available to re-evaluate imazamethabenz-methyl. Thus, appropriate dermal and inhalation exposures were estimated using the Pesticide Handlers Exposure Database (PHED), Version 1.1. PHED is a compilation of generic mixer/loader and applicator passive dosimetry data with associated software that facilitates the generation of scenario-specific exposure estimates based on formulation type, application equipment, mix/load systems and the level of personal protective equipment.

In some cases, PHED did not contain exact data sets to estimate exposure to workers. In those cases surrogate data were used. Exposure for mixing and loading emulsifiable concentrate and mixing and loading suspension were estimated using the data for liquids. Exposure for mixing and loading soluble granules was estimated using the dry flowable data.

PHED unit exposures coupled with information on the amount of imazamethabenz-methyl handled per day was used to estimate handler exposure. The amount handled per day is based upon the maximum label application rate and default assumptions on the area (of crop) which can reasonably be treated in one day.

Calculated MOEs (summarized Appendix V, Table 1) exceed the target MOE for all exposure scenarios and are not of concern. Proposed mitigation measures and regulatory actions are described in Section 8.0.

3.2.2.2 Postapplication Worker Exposure and Risk Assessment

The postapplication occupational risk assessment considered exposures to workers entering treated agricultural sites to conduct activities involving foliar contact. Based on the imazamethabenz-methyl use pattern, there is a potential for short-term (1 to 30 days) postapplication exposure to imazamethabenz-methyl residues for workers.

Chemical-specific dislodgeable foliar residue (DFR) data and activity-specific transfer coefficients (TC) can be used to estimate postapplication exposure resulting from contact with treated foliage at various times after application. DFR data include the amount of residue that can be dislodged or transferred from a surface, such as the leaves of a plant. A TC is a factor that relates worker exposure to dislodgeable residues. TCs are specific to a given crop and activity combination (e.g. hand harvesting apples, scouting late-season cotton) and reflect standard agricultural work clothing worn by adult workers. Postapplication exposure activities for imazamethabenz-methyl include scouting, swathing and harvesting.

For workers entering a treated site, restricted-entry intervals (REIs) are calculated to determine the minimum length of time required before people can safely re-enter. An REI is the duration of time that must elapse before residues decline to a level where performance of a specific activity results in exposures above the target MOE (i.e. > 100 for short-term exposure scenarios).

Although imazamethabenz-methyl is applied to agricultural areas including terrestrial feed and food crops, no relevant DFR studies were available. As a result, a conservative default value of 20% of the application rate with a 10 % dissipation per day was used.

The postapplication risk estimates include a number of conservative inputs, such as the assumption that workers are exposed to residues following the maximum number of applications (only one in this case) at the maximum rate.

Calculated MOEs exceed the target MOE on day zero and are therefore not of concern. The proposed REIs are set at 12 hours. Postapplication exposure calculations for each use site are summarized in Appendix V, Table 2.

3.2.3 Non-occupational Exposure and Risk

3.2.3.1 Non-occupational Handler and Risk

There are no domestic class products; therefore, a non-occupational handler assessment was not required.

3.2.3.2 Bystander Exposure and Risk

For bystanders, exposure is expected to be much less than that of field workers and is considered negligible.

3.3 Dietary Risk Assessment

In a dietary exposure assessment, the PMRA determines how much of a pesticide residue, including residues in milk and meat, may be ingested with the daily diet. Exposure to imazamethabenz-methyl from potentially treated imports is also included in the assessment. These dietary assessments are age specific and incorporate the different eating habits of the population at various stages of life. For example, the assessments take into account differences in children's eating patterns, such as food preferences and the greater consumption of food

relative to their body weight when compared to adults. Dietary risk is then determined by the combination of the exposure and the toxicity assessments. High toxicity may not indicate high risk if the exposure is low. Similarly, there may be risk from a pesticide with low toxicity if the exposure is high.

The PMRA considers limiting the use of a pesticide when its risk exceeds 100% of the reference dose. Science Policy Notice SPN2003-03, *Assessing Exposure from Pesticides, A User's Guide*, presents detailed acute and chronic risk assessments procedures.

Residue estimates used in the dietary risk assessment may be conservatively based on the maximum residue limits (MRL). They may also be based on the field trial data representing the residues that may remain on food after treatment at the maximum label rate. Surveillance data representative of the national food supply may also be used to derive a more accurate estimate of residues that may remain on food when it is purchased. These include the Canadian Food Inspection Agency's National Chemical Residue Monitoring Program and the United States Department of Agriculture Pesticide Data Program.

Chronic dietary risk assessments were conducted using the Dietary Exposure Evaluation Model (DEEM–FCID™, Version 2.03), which uses updated food consumption data from the United States Department of Agriculture's Continuing Surveys of Food Intakes by Individuals, 1994–1996 and 1998.

For more information on dietary risk estimates or residue chemistry information used in the dietary assessment, see Appendix VI and VII.

3.3.1 Determination of Acute Reference Dose

An acute reference dose was not calculated as there was not an endpoint of concern, due to the low acute toxicity of imazamethabenz-methyl.

3.3.2 Acute Dietary Exposure and Risk Assessment

No acute dietary exposure and risk assessment was conducted as no acute reference dose was determined.

3.3.3 Determination of Acceptable Daily Intake

To estimate the dietary risk from repeat exposures, the most suitable study was a two-year chronic dietary toxicity study on the rat. This study resulted in a NOAEL of 12.5 mg/kg bw/day based on an increased incidence of hepatocellular degeneration along with transient alterations in hepatic enzyme levels in males and statistically significant decreased body weights and body-weight gains in females at the lowest observed adverse effect level (LOAEL) of 50 mg/kg bw/day. Standard uncertainty factors of 10-fold for interspecies extrapolation and 10-fold for intraspecies variability were used.

The *Pest Control Products Act* factor was reduced to 1-fold as the toxicity database was considered complete and there was a low level of concern for potential prenatal and postnatal toxicity with imazamethabenz-methyl.

$$\text{ADI} = \frac{\text{12.5 mg/kg bw/day}}{\text{100}} = \text{0.125 mg/kg bw/day}$$

This ADI provides a margin of 4000 to the lowest NOAEL for postimplantation losses noted in rabbits. It is thus considered protective of all populations including pregnant women, infants and children.

3.3.4 Chronic Dietary Exposure and Risk Assessment

The chronic dietary risk was calculated by using the average consumption of different foods and the average residue values on those foods. This expected intake of residues was then compared to the ADI. When the expected intake of residues is less than the ADI, then chronic dietary exposure is acceptable.

Deterministic chronic dietary exposure analyses were performed to determine the exposure and risk estimates resulting from the registered agricultural commodities. Maximum residue limits as well as empirical processing factors (DEEM defaults) were used.

The chronic potential daily intake accounted for less than 1% of the ADI for all subpopulations and is, therefore, not of concern.

3.3.5 Cancer Assessment

A cancer risk assessment was not conducted because the imazamethabenz-methyl database did not suggest any carcinogenic potential in mice or rats.

3.4 Exposure From Drinking Water

3.4.1 Concentrations in Drinking Water

Imazamethabenz-methyl residues in potential drinking water sources were estimated using modelling data. The chronic estimated drinking water concentration calculated from the exposure model is 329 ppb.

3.4.2 Drinking Water Exposure and Risk Assessment

Drinking water estimates were incorporated directly in the exposure model. For more information, please refer to the aggregate risk assessment (Section 3.5).

3.5 Aggregate Risk Assessment

Aggregate exposure is the total exposure to a single pesticide that may occur from food, drinking water, residential and other non-occupational sources as well as from all known or plausible exposure routes (oral, dermal and inhalation).

As there are no residential or other non-occupational uses of imazamethabenz-methyl, aggregate exposure is from dietary and drinking water exposures only.

Deterministic aggregate chronic (food and water) exposures accounted for less than 23% of the ADI for all subpopulations and is, therefore, not of concern.

4.0 Impact On the Environment

4.1 Fate and Behaviour in the Environment

Based on its physical-chemical properties (Section 2.2), imazamethabenz-methyl is very soluble in water. It has a very low potential for volatilization from moist soils or water surfaces under field conditions and is not likely to bioaccumulate in organisms. Environmental fate data for imazamethabenz-methyl are summarized in Appendix VIII, Table 1. Imazamethabenz-methyl is relatively stable to hydrolysis at pH 5, slow at pH 7 and rapid at pH 9. Phototransformation is not a major route of transformation in acidic soil. However, it could play a significant role in acidic and neutral water at medium temperature (19°C).

Imazamethabenz-methyl is slightly persistent to persistent in soil under aerobic and anaerobic conditions with half-lives ranging from 135 to 234 days. The rate of aerobic soil biotransformation is dependent upon temperature and moisture content. Warmer and moderate moist soils (40% maximum water holding capacity) tend to degrade imazamethabenz-methyl more rapidly than cooler and wetter soil. The major transformation product is imazamethabenz-methyl acid. Canadian field dissipation studies resulted in half-lives different from those determined in laboratory studies, with values ranging from 21 to 137 days, indicating that imazamethabenz-methyl is slightly persistent to moderately persistent in soils.

In the aquatic aerobic environment, imazamethabenz-methyl is non-persistent to moderately persistent based on studies conducted at neutral pH. Imazamethabenz-methyl acid is the major transformation product, which is non-persistent in water.

Imazamethabenz-methyl does not bind strongly to soil and sediment but rather partitions mainly to aqueous phase. Laboratory studies on adsorption/desorption and soil column leaching studies indicate that imazamethabenz-methyl and the major transformation product imazamethabenz-methyl acid have a potential to be highly mobile. In terrestrial field studies conducted in Canada, varying degrees of leaching have been identified. The extent of leaching for imazamethabenz-methyl and its major transformation product is related to cation exchange capacity, organic matter content and texture. The potential for leaching is prominent in low organic and clay loam soils because of increased solubility and decreased adsorption. However, field dissipation studies showed no leaching of imazamethabenz-methyl beyond a depth of 15 cm.

Canadian water monitoring data show detection of imazamethabenz-methyl in surface water with concentrations ranging from 0.0003 to 12.0 µg/L (Appendix IX). At present, no monitoring data is available for groundwater.

4.2 Effects on Non-target Species

The environmental risk assessment integrates the environmental exposure and ecotoxicology information to estimate the potential for adverse effects on non-target species. This integration is achieved by comparing exposure concentrations with concentrations at which adverse effects occur. Estimated environmental exposure concentrations (EECs) are concentrations of pesticide in various environmental media, such as food, water, soil and air. The EECs are estimated using standard models which take into consideration the application rate(s), chemical properties and environmental fate properties, including the dissipation of the pesticide between applications. Ecotoxicology information includes acute and chronic toxicity data for various organisms or groups of organisms from both terrestrial and aquatic habitats including invertebrates, vertebrates and plants. Toxicity endpoints used in risk assessments may be adjusted to account for potential differences in species sensitivity as well as varying protection goals (i.e. protection at the community, population or individual level).

Initially, a screening level risk assessment is performed to identify pesticides or specific uses that do not pose a risk to non-target organisms, and to identify those groups of organisms for which there may be a potential risk. The screening level risk assessment uses simple methods, conservative exposure scenarios (e.g. direct application at a maximum cumulative application rate) and sensitive toxicity endpoints. A risk quotient (RQ) is calculated by dividing the exposure estimate by an appropriate toxicity value (RQ = exposure/toxicity), and the risk quotient is then compared to the level of concern (LOC = 1). If the screening level risk quotient is below the level of concern, the risk is considered negligible and no further risk characterization is necessary.

If the screening level risk quotient is equal to or greater than the level of concern, then a refined risk assessment is performed to further characterize the risk. A refined assessment takes into consideration more realistic exposure scenarios (such as drift to non-target habitats) and might consider different toxicity endpoints. Refinements may include further characterization of risk based on exposure modelling, monitoring data, results from field or mesocosm studies, and probabilistic risk assessment methods. Refinements to the risk assessment may continue until the risk is adequately characterized or no further refinements are possible.

4.2.1 Effects on Terrestrial Organisms

Assessment of the risk of imazamethabenz-methyl to terrestrial organisms was based upon an evaluation of its toxicity to earthworms (acute contact), bees (acute contact), 2 species of birds (acute oral, dietary and chronic), 2 species of mammals (acute oral, sub chronic and chronic) and 50 species of terrestrial plants (vegetative vigour). A summary of terrestrial toxicity data for imazamethabenz-methyl is presented in Appendix VIII, Table 2. For the assessment of risk, toxicity endpoints chosen from the most sensitive species were used as surrogates for the wide range of species that can be potentially exposed following treatment with imazamethabenz-methyl.

For birds and mammals, the most sensitive endpoints (acute oral, dietary and reproduction) were used to extrapolate toxicity endpoints for birds and mammals of different sizes (20, 100 and 1000 g for birds and 15, 35 and 1000 g for mammals). To address differences in species sensitivity, the acute oral lethal dose to 50% (LD_{50}) and dietary lethal concentration to 50% (LC_{50}), converted to daily dose, were further divided by a safety factor of 10. The screening level assessment used relevant food categories representing specific feeding guilds for each bird and mammal size class consisting of 100% of a particular dietary item (e.g. plants, grain/seeds, insects and fruit). Estimated dietary exposures (EDE) for each bird and mammal size were calculated based on EECs for each feeding preference group at each application rate and food ingestion rates.

As no small birds in North America are known to eat a diet primarily of leafy plant material or grass, EDEs for small birds (20 and 100 g) based on a 100% diet of plants were not calculated. The risk quotient in the screening assessments of large birds representing the herbivore guild was the only one to exceed the level of concern (LOC) by a factor of 1.2 (RQs greater than 1). For mammals, the LOC was reached with RQ = 1.0 and was represented by small mammals from the herbivore food guild. However, the screening level herbivore diet consists of 100% contaminated leaves and leafy crops which have a very high water content and are unlikely to make up 100% of an herbivore diet. Other vegetation types were examined, including short range grass, long grass and forage crops. Risk quotients based on these vegetation types did not exceed the LOC. Additional conservatisms in the risk assessment include the assumption that 100% of the diet will be contaminated at maximal estimated residue levels. It is likely that some of the diet will be obtained from non-contaminated areas, and that residues are not likely to be at the maximal estimated level on all food items. Overall, negligible risks are expected to be posed to birds and mammals.

Imazamethabenz-methyl demonstrated no adverse toxicological effects on terrestrial invertebrates, birds or mammals on an acute oral, dietary and reproductive basis. As imazamethabenz-methyl is a herbicide, adverse effects to non-target terrestrial plants are expected. Vegetative vigour studies indicated that, although many plant species grew successfully, some species did not follow normal growth patterns and that detrimental effects (failure to recover) were observed at a low application rate. The effects are likely due to the ability of imazamethabenz-methyl to inhibit the plant enzyme acetolactate synthase, hence stopping cell division and plant growth by blocking branched chain amino acid biosynthesis.

No toxicity studies conducted with transformation products were available for review, except for one study with the acid on effects on mammals.

The screening level risk assessment indicated that exposure to imazamethabenz-methyl does not pose a risk to terrestrial invertebrates, mammals and birds. Appendix VIII, Tables 3 and 4, summarizes the risk assessment from imazamethabenz-methyl to terrestrial organisms.

The imazamethabenz-methyl herbicide poses a risk to non-target terrestrial plants. The LOC was exceeded by 11 times at the lowest application rate (250 g a.i./ha) for the black nightshade plant and 1.7 times for the transplanted rice known as an emerged aquatic vascular plant. Less than 9% of the imazamethabenz-methyl application rate (250–500 g a.i./ha) is expected to negatively affect non-target terrestrial plants (concentration effective against 25% of test organisms divided by the application rate). As a result, a refinement of the risk assessment was conducted taking into consideration the concentrations of imazamethabenz-methyl that could be present in terrestrial habitat directly adjacent to the treated field through spray drift. Spray drift data for a medium American Society of Agricultural Engineers droplet size, as is generally used in ground boom applications of herbicides, indicates that the maximum amount of spray that will drift one metre down wind from the point of application during spraying is 6%.

Using this percent drift, the off-site EECs for imazamethabenz-methyl were calculated but used the highest application rate. Based on this refinement to the assessment, imazamethabenz-methyl was found to pose a risk to non-target terrestrial plants directly adjacent to the application field. Exceedance of the LOC was eliminated for the transplanted rice, but was only reduced to 1.3 times from 11 times at the highest application rate for the black nightshade. Buffer zones will be required to mitigate the risk of imazamethabenz-methyl to non-target terrestrial plants. Appendix VIII, Table 5, summarizes the refined risk assessment of imazamethabenz-methyl to non-target terrestrial plants.

4.2.2 Effects on Aquatic Organisms

Acute and chronic risk was based on an evaluation of toxicity data on imazamethabenz-methyl for seven freshwater species (one invertebrate, three fish, one alga and two vascular plants). No toxicity data on the transformation products were available for aquatic studies. A summary of aquatic toxicity data for imazamethabenz-methyl is presented in Appendix VIII, Table 2. For the risk assessment, toxicity endpoints chosen from the most sensitive species were used as surrogates for the wide range of species that can be potentially exposed following treatment with imazamethabenz-methyl. The endpoints were derived by dividing the EC_{50} (median effective concentration) or LC_{50} from the appropriate laboratory study by a factor of 2 for aquatic invertebrates and plants, and by a factor of 10 for fish and amphibians (based on surrogate data from fish studies).

Based on acute and chronic toxicity, imazamethabenz-methyl is of negligible risk to freshwater invertebrates, fish and algae. No toxicity data were available for estuarine/marine fish or algae species. As imazamethabenz-methyl is a herbicide and adverse effects to non-target aquatic plants are expected. Imazamethabenz-methyl significantly affected biomass of duckweed and posed a limited risk to transplanted rice (treated as a non-target terrestrial plant).

The risk assessment was conducted using data for the most sensitive freshwater organisms tested. These are the *Daphnia magna*, bluegill sunfish, and rainbow trout, fathead minnow, algae, aquatic immersed plant (duckweed), aquatic emerged plant (transplanted rice) and a surrogate fish species for amphibian (i.e. the early life stage of the fathead minnow).

The screening level risk assessment presented in Appendix VIII, Table 6 indicated that imazamethabenz-methyl does not pose a risk to freshwater invertebrates, fish and algae. However, a potential risk to the vascular plant duckweed and the amphibians was identified at the highest application rate. The LOC was exceeded by 1.73 times at an application rate of 0.5 kg a.i./ha for the duckweed and by 1.03 for amphibians. Thus, a refined risk assessment was triggered, which reduced the exceedance of the LOC to 0.11 times from spray drift for the duckweed and 0.61 times for amphibians (Appendix VIII, Table 7). Risk quotients presented in Appendix VIII, Table 8, for the immersed aquatic vascular plant determined for imazamethabenz-methyl in runoff, were less that 1, thus indicating that the level of concern was not exceeded for duckweed. Water monitoring data were used in the environmental risk assessment to estimate the EEC ^{90th} percentile (of the 96 hour average) for British Columbia, Saskatchewan and Manitoba where imazamethabenz-methyl is expected to be used (see Appendix IX for more explanation).

5.0 Value

5.1 Commercial Class Products

5.1.1 Commercial Class Alternatives to Imazamethabenz-Methyl

All imazamethabenz-methyl uses are supported by the registrant. There are no risk concerns for any of the registered uses. Consequently, the availability of alternatives to the use of imazamethabenz-methyl were not considered.

5.2 Domestic Class Products

In Canada, there are no registered Domestic Class products containing imazamethabenz-methyl.

5.3 Value of Imazamethabenz-Methyl

Wild oats is one of the most troublesome weeds, especially in the Prairie provinces. It is very competitive with wheat and barley and if left unchecked, 10 wild oats per square metre can reduce wheat and barley yields by 10%. In the Prairie provinces and the Peace River region, the Okanagan Valley and the Creston Flats areas of British Columbia, imazamethabenz-methyl is one of few herbicides that effectively controls wild oats and some broadleaf weeds in cereals (including spring and durum wheat, and spring barley). In addition, imazamethabenz-methyl is one of two herbicides used to control wild mustard and stinkweed in sunflower and annual ryegrass grown only for seed. Moreover, imazamethabenz-methyl can be tank-mixed with other herbicides to broaden the spectrum of weed control.

In the early 1990s, the estimated average annual losses caused by weeds were $280.8 million in wheat, $61 million in barley and $2.1 million in sunflower in Western Canada. Imazamethabenz-methyl was reported to be used on these crops to prevent and reduce a portion of the economic losses incurred by weeds.

Although populations of imazamethabenz-methyl-resistant wild oats have been identified in Canada, imazamethabenz-methyl can readily be used in locations lacking resistant populations in rotation with other herbicide groups including Groups 1, 3, 8, 9, 10, 11 or 16 to mitigate resistance development in populations of wild oats. The mode of action of imazamethabenz-methyl (being a Group 2 herbicide) plays a role in managing resistance development to other herbicide groups.

6.0 Toxic Substances Management Policy Considerations

The management of toxic substances is guided by the federal government's TSMP, which puts forward a preventive and precautionary approach to deal with substances that enter the environment and could harm the environment or human health. The policy provides decision makers with direction and sets out a science-based management framework to ensure that federal programs are consistent with its objectives. One of the key management objectives is virtual elimination from the environment of toxic substances that result predominantly from human activity and that are persistent and bioaccumulative. These substances are referred to in the policy as Track 1 substances.

During the review process, imazamethabenz-methyl was assessed in accordance with the PMRA Regulatory Directive DIR99-03, *The Pest Management Regulatory Agency's Strategy for Implementing the Toxic Substances Management Policy*. Substances associated with the use of imazamethabenz-methyl were also considered, including major transformation products formed in the environment (see Appendix VIII, Table 9), microcontaminants in the technical product and formulants in the end-use products. The PMRA reached the following conclusions.

- The log *n*-octanol–water partition coefficient (log K_{ow}) of imazamethabenz-methyl ranges from 1.54 to 1.82, which is below the TSMP Track-1 cut-off criterion for log $K_{ow} \geq 5.0$. Imazamethabenz-methyl does not meet the criterion for persistence in water as its half-life values in water (ranging from 7 to 160 days) are below the TSMP Track 1 cut-off criterion for water (≥ 182 days). However imazamethabenz-methyl does meet the criterion for persistence in soil because the half-life determined for imazamethabenz-methyl in soil (ranging from 135 to 234 days) is above the TSMP Track 1 cut-off for soil (≥182 days). The vapour pressure and Henry's law constant indicate that imazamethabenz-methyl will not volatilize from water or moist soil under field conditions; thus, long-range atmospheric transport of imazamethabenz-methyl is not likely to occur.

- End-use products containing imazamethabenz-methyl do not contain any formulants of health or environmental concern identified in the *Canada Gazette*, Part II, Volume 139, Number 24, pages 2641–2643: *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern*.

- Technical grade imazamethabenz-methyl does not contain any contaminants of health or environmental concern identified in the *Canada Gazette*, Part II, Volume 139, Number 24, pages 2641–2643: *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern.*

Therefore, the use of imazamethabenz-methyl is not expected to result in the entry of Track 1 substances into the environment.

7.0 Summary

7.1 Human Health and Safety

The toxicology database submitted for imazamethabenz-methyl is adequate to define the majority of toxic effects that may result from human exposure to imazamethabenz-methyl. Imazamethabenz-methyl was not carcinogenic, genotoxic, neurotoxic or teratogenic in rats or rabbits. When imazamethabenz-methyl was given to pregnant animals, the developing fetus was no more sensitive to it than the adult animal. The liver was the main target of toxicity in rats. The first signs of toxicity in dogs given daily doses of imazamethabenz-methyl over longer periods of time were slight changes in hematology along with increased liver, spleen and heart weights and decreased body weight. In mice, increases in thyroid/parathyroid and adrenal weights were noted at high doses. The risk assessment protects against these effects by ensuring that the level of human exposure is well below the lowest dose at which these effects occurred in animal tests.

7.1.1 Occupational Risk

The occupational application and postapplication risks are acceptable for the exposure scenarios involving the use of imazamethabenz-methyl. The calculated margins of exposure for application and postapplication occupational exposures are all above the Agency's target assuming that workers wear baseline personal protective equipment.

7.1.2 Dietary Risk from Food and Water

The aggregate chronic (food and water) risk assessments demonstrate that there were no dietary concerns for any population subgroup in Canada, including infants, children, teenagers, adults and seniors. In addition, no dietary concerns were evident for nursing or pregnant females or based on gender in general.

7.1.3 Dietary Risk from Drinking Water

The potential for the contamination of drinking water with imazamethabenz-methyl is expected to be minimal.

7.1.4 Non-occupational Risk

Imazamethabenz-methyl is not registered for use in any residential areas, therefore, a non-occupational risk assessment was not required.

7.2 Environmental Risk

Imazamethabenz-methyl is slightly persistent to persistent in most soils and non-persistent to moderately persistent in aquatic systems. Imazamethabenz-methyl is mobile and may occur in runoff and surface waters at very low concentrations. A screening level risk assessment indicates that it is not a risk to terrestrial and aquatic organisms, except for plants. A refined risk assessment for non-target terrestrial and aquatic plants indicates that spray drift will have adverse effects on non-target terrestrial plants only. The risk quotients in the refined assessments of non-target terrestrial plants exceeded the level of concern by a factor of 1.3 (RQs greater than 1), but remained under level of concern (RQ less than 1) for the aquatic plants.

7.3 Value

From the value perspective, imazamethabenz-methyl is acceptable for continued registration.

8.0 Proposed Regulatory Decision

An evaluation of current scientific data from the applicant, scientific reports and information from other regulatory agencies determined that, under the proposed conditions of use, imazamethabenz-methyl does not present an unacceptable risk to human health or the environment.

8.1 Proposed Regulatory Actions

8.1.1 Proposed Regulatory Action Related to Human Health

The PMRA has determined that the dietary and drinking water risks and the worker risks during mixing, loading and application are acceptable for all uses, provided that the following mitigation measures are implemented.

8.1.1.1 Proposed Mitigation for Mixer, Loader and Applicator Exposure

For all formulations, the following mitigation measures and label statements are proposed.

- Mixers, loaders and applicators must wear a long-sleeved shirt, long pants, shoes and socks and chemical-resistant gloves (gloves not required for groundboom sprayers).
- Do not re-enter treated fields until 12 hours after application.
- Apply only when the potential for drift to areas of human habitation or areas of human activity (houses, cottages, schools and recreational areas) is minimal. Take into consideration wind speed, wind direction, temperature, application equipment and sprayer settings.

8.1.1.2 Residue Definition for Risk Assessment and Enforcement

Division 15, Table II, of the Food and Drug Regulations currently provides no definition for the residue of concern. It is recommended that the residue definition for risk assessment and enforcement purposes for plant commodities be defined as the para- and meta isomers of parent methyl ester and their acid metabolites, based on plant metabolism studies.

For more information on the definition of the residue of concern for imazamethabenz-methyl, see Appendix VII.

8.1.1.3 Maximum Residue Limits for Imazamethabenz-Methyl in Food

In general, when the re-evaluation of a pesticide has been completed, the PMRA intends to update Canadian maximum residue limits and to remove MRLs that are no longer supported. The PMRA recognizes, however, that interested parties may want to retain an MRL in the absence of a Canadian registration to allow legal importation of treated commodities into Canada. The PMRA requires similar chemistry and toxicology data for such import MRLs as those required to support Canadian food use registrations. In addition, the PMRA requires residue data that are representative of use conditions in exporting countries, in the same manner that representative residue data are required to support domestic use of the pesticide. These requirements are necessary so that the PMRA may determine whether the requested MRLs are needed and to ensure they would not result in unacceptable health risks.

Division 15, Table II, of the Food and Drug Regulations currently provides no definition for the residue of concern for imazamethabenz-methyl and no MRLs are specified. The supported food uses of imazmethabenz-methyl are on wheat, barley and sunflower. Where no specific MRL is established for a pest control product under the Food and Drug Regulations, subsection B.15.002(1) applies. This requires that residues do not exceed 0.1 ppm, which is considered a general MRL for enforcement purposes. However, changes to this general MRL may be implemented in the future, as indicated in Discussion Document DIS2006-01, *Revocation of 0.1 ppm as a General Maximum Residue Limit for Food Pesticide Residues [Regulation B.15.002(1)]*. If and when the general MRL is revoked, a transition strategy will be established to allow permanent MRLs to be set for barley, wheat and sunflower.

With the exception of barley hay and wheat (hay and forage), residue data were available to indicate that existing MRLs should not be exceeded if imazamethabenz-methyl is used according to good agricultural practice, as stipulated on the current product labels. MRLs are proposed based on the fact that no residues were detected during field trials conducted in Canada and abroad and based on the sensitivity of the analytical method.

Table 8.1.1.3 Proposed Imazamethabenz-Methyl MRLs for Commodities Registered in Canada

Commodity	MRL (ppm)
Barley grain	0.1
Wheat grain	0.1
Sunflower seed	0.1

Parties interested in supporting MRLs for residues of imazamethabenz-methyl should contact the PMRA during the comment period of this document to discuss the submission of appropriate data. For supplemental MRL information regarding the international situation and trade implications, refer to Appendix X.

8.1.2 Proposed Regulatory Action Related to Environment

The risk assessment has indicated adverse effects on non-target terrestrial plants. To reduce the effects of imazamethabenz-methyl in the environment, mitigation in the form of precautionary label statements and spray buffer zones are required. Environmental mitigation statements and spray buffer zones are listed in Appendix XI.

8.1.3 Proposed Regulatory Action Related to Value

Amendment(s) to the labels arising from the re-evaluation of imazamethabenz-methyl are proposed in Appendix XI.

8.2 Additional Data Requirements

No additional data are required for imazamethabenz-methyl at this time.

List of Abbreviations

♂	males
♀	females
↑	increased
↓	decreased
λ	wavelength
°C	centigrade (Celsius)
^{14}C	radioactive isotope 14 of the carbon atom
µCi	microCurrie(s)
µg	microgram(s)
ALS	acetolactate synthase
amu	atomic mass unit
AR	applied radioactivity
ASAE	American Society of Agricultural Engineers
ASS	imazamethabenz-methyl
BCF	bioconcentration factor
bw	body weight
bwg	body-weight gain
BWI	body weight (fresh weight) of an individual [kg bw/ind]
C	concentration
CAF	composite assessment factor
CAS	chemical abstract society
CFIA	Canadian Food Inspection Agency
CHO	Chinese hamster ovary
CI	confidence interval
cm	centimetre(s)
cm^2	squared centimetre
d	day(s)
DEEM®	Dietary Exposure Evaluation Model
DER	data evaluation report
DFR	dislodgeable foliar residue
DNA	deoxyribonucleic acid
DRA	dietary risk assessment
DT_{50}	dissipation time to 50% (the dose required to observe a 50% decline in the test population)
DU	dust or powder
EC	effective concentration emulsifiable concentrate or emulsion
EC_{25}	concentration effective against 25% of test organisms [mg a.i./kg diet or mg a.i./L]
EC_{50}	median effective concentration [mg a.i./kg diet or mg a.i./L]
EDE	estimated dietary exposures
EEC	expected environmental concentration [mg a.i./kg diet or mg a.i./L or mg a.i./kg soil]
F_0	parental animals
F_1	first filial generation

g	gram(s)
GC	gas chromatography
GGT	gamma-glutamyl transpeptidase
ha	hectare(s)
Hct	hematocrit
Hgb	hemoglobin
HPLC	high performance liquid chromatography
hr	hour(s)
IUPAC	International Union of Pure and Applied Chemistry
K_{oc}	organic carbon adsorption coefficient (a.k.a. organic carbon partition coefficient; soil sorption constant) [mL/g *or* complex]
K_{ow}	*n*-octanol–water partition coefficient
Kg	kilogram(s)
L	litre(s)
LC	liquid concentrate
LC_{50}	lethal concentration to 50% (a concentration causing 50% mortality in the test population [mg a.i./kg diet *or* mg a.i./L]
LD_{50}	lethal dose to 50% (a dose causing 50% mortality in the test population) [mg a.i./kg bw]
LOAEL	lowest observed adverse effect level
LOC	level of concern
M	Molar [6.02×10^{23} particle]
m	metre(s)
—	meta
mg	milligram(s)
M/L	mixer/loader
M/L/A	mixing/loading/applying
mL	millilitre(s)
MOE	margin of exposure
mPa	milliPascal(s)
MRL	maximum residue limit
MS	mass spectrometry
MTDB	maximum theoretical dietary burden
N/S	not specified
N	normality [expressed as the number of equivalent of a substance ÷ number of litre of solution]
nm	nanometre(s)
NOAEL	no observable adverse effect level
NOEC	no observed effect concentration [mg a.i./kg diet *or* mg a.i./L]
NOEL	no observable effect dose level [mg a.i./kg bw]
OM	organic matter content
p-	para
PCP	Pest Control Product
PDP	Pesticide Data Program (United States data)
pH	$-\log_{10}$ hydrogen ion concentration
PHED	Pesticide Handlers Exposure Database
pK_a	-log10 acid dissociation constant

PMRA	Pest Management Regulatory Agency
ppb	parts per billion
PPE	personal protective equipment
ppm	parts per million [mg/kg] *or* [μL/L] or [mg/L]
PRVD	Proposed Re-evaluation Decision
RA	risk assessment
RBC	red blood cell(s)
REI	restricted-entry interval
RQ	risk quotient (equivalent to EEC ÷ endpoint value)
SAP	serum alkaline phosphatase
SG	soluble granules
SGOT	aspartate aminotransferase
SGPT	alanine aminotransferase
SRL	safe residue limit
SU	suspension
T	temperature
TC	transfer coefficient
TRR	total radioactive residue(s)
TSMP	Toxic Substances Management Policy
UV	ultraviolet
w/v	weight per volume
wts	body weights

Appendix I Registered Products Containing Imazamethabenz-Methyl[1]

Registration Number	Marketing Class	Registrant	Product Name	Formulation Type	Guarantee
20568	Commercial	Nufarm Agriculture Inc.	ASSERT 300LC Herbicide	Emulsifiable concentrate or Emulsion	300 g/L
21032	Commercial	Nufarm Agriculture Inc.	ASSERT 300 SC Agricultural Herbicide	Suspension	300 g/L
25618	Commercial	Nufarm Agriculture Inc.	ASSERT SG Herbicide	Soluble granules	67%
20567	Technical	Nufarm Agriculture Inc.	ASSERT Technical Herbicide	Dust or Powder	95.1%

[1] Excluding discontinued products or products with a submission for discontinuation as of 21 April 2008.

Appendix II Registered Commercial Class Uses of Imazamethabenz-Methyl In Canada As of 21 April 2008[1]

Use-Site Category	Site(s)		Weeds	Formulation Type[2]	Maximum Application Rate (g a.i./ha)
7, 13, and 14 Industrial Oil Seed Crops and Fibre Crops, Terrestrial Feed Crops and Terrestrial Food Crops	Sunflower	For Prairie provinces	Wild mustard and stinkweed	EC SU SG	250 250 250
13 and 14 Terrestrial Feed Crops and Terrestrial Food Crops	Spring wheat	For Prairie provinces and Peace River region, Okanagan Valley and Creston Flats areas of British Columbia	Wild oats, wild mustard, stinkweed, wild buckwheat and tartary buckwheat	EC SU SG	480 480 500
13 and 14 Terrestrial Feed Crops and Terrestrial Food Crops	Durum wheat	For Prairie provinces and Peace River region of British Columbia only	Wild oats, wild mustard, stinkweed, wild buckwheat and tartary buckwheat	EC SU SG	480 480 500
13 and 14 Terrestrial Feed Crops and Terrestrial Food Crops	Spring barley	For Prairie provinces and Peace river region, Okanagan Valley and Creston Flats areas of British Columbia	Wild oats, wild mustard, stinkweed, wild buckwheat and tartary buckwheat	EC SU SG	480 480 500
14 Terrestrial Food Crops	Annual ryegrass grown only for seed	For Prairie provinces	Wild mustard and stinkweed	SU	480

1 All uses were supported by the registrant. Application is made once per year by ground equipment only. No aerial application is allowed for any uses. Information on application equipment and the number of applications is based on both label use information and information provided by the registrant under DACO 5.2. Uses of tank mix products including pre-packaged tank mixes are not presented.

2 EC = Emulsifiable concentrate or emulsion, SG = Soluble granules, SU = Suspension

Appendix III Toxicology Profile of Technical Imazamethabenz-Methyl and Its Isomers

NOTE: Effects noted below are known or assumed to occur in both sexes unless otherwise specified.

Study/Species/ # of Animals Per Group	Dose Levels/Purity of Test Material	NOAEL (mg/kg bw/day)	Results/Effects
Metabolism/Toxicokinetic Studies			
AC 222,293 Technical			
Absorption, Distribution, Metabolism & Excretion, Single Oral Dose - Sprague-Dawley Rats (Para: 11♂, Meta: 13♂)	• Single oral dose of 25 mg/kg bw (para (19.3 mcCi/mg) & meta (18.9 mcCi/mg) isomers) in corn oil • 99% purity		**Distribution**: Para isomer: Maximum tissue levels were found in the liver (0.44 ppm), kidney (0.06 ppm), fat (0.06 ppm), muscle (0.05 ppm) and blood (0.04 ppm) at 24 hours. All of the tissue levels were less than 0.05 ppm at 96 hours. Meta isomer: Maximum tissue levels were found in the liver (0.33 ppm), kidney (0.27 ppm), fat (0.13 ppm), muscle (0.12 ppm) and blood (0.39 ppm) at 24 hours. All of the tissue levels were less than 0.05 ppm at 48 hours. **Metabolism**: Para isomer: The major metabolites in tissue extracts were mainly the acid CL 252,768 and its p-hydroxymethyl analog, CL 119,543, which accounted for 89.7 and 5.8% of the extractable activity, respectively, in liver, 16.9 and 58.5% in muscle and 16.3 and 77.2% in fat. The major urinary metabolites were CL 252,768 (the acid) accounting for 79.2%, CL 119,543 (its p-hydroxymethyl analog) accounting for 12.1%, CL 119,544 accounting for 2.6% and the remainder were unknown. Meta isomer: The major metabolites in tissue extracts were mainly the acid CL 222,575 and CL 119,610, which accounted for 65.2 and 4.2% of the extractable activity, respectively, in liver, 42.0 and 13.6% in the kidneys, 45.9 and 45.2% in muscle and 81 and 17.6% in fat. The major urinary metabolites were CL 222,575 accounting for 82.7%, CL119,610 accounting for 4.4%, CL 119,611 accounting for 3.2%, an unknown accounted for 5.2% & the remainder were unknown. Proposed metabolic pathway: The major metabolic processes are the hydrolytic cleavage of the methyl ester linkage and hydroxylation of the methyl group in the benzene ring. This leads to the formation of the parent acid as the major metabolite, and hydroxymethyl analog of the acid, and hydroxymethyl analogs of the parent esters as the minor metabolites. **Excretion**: Para isomer: A total of 77.6% & 18.7% of the dose was excreted in the urine and feces at 0 to 24 hrs, 0.8% & 1.6% at 24 to 48 hrs, 1.3% & 0.2% at 48 to 96 hours and 0.2% & 0.2%, respectively, at 96 to 192 hrs. Cage wash accounted for 1.2%.

Study/Species/ # of Animals Per Group	Dose Levels/Purity of Test Material	NOAEL (mg/kg bw/day)	Results/Effects
			Meta isomer: The figures were essentially identical with those of the para isomer, 76.8% & 12.7% of the meta-isomer dose was excreted in the urine and feces during the first 24 hrs. Total recovery was 101.8% & 101.5% for the para and meta isomers, respectively.
Absorption, Distribution, Metabolism & Excretion, Single Intravenous or Oral Dose - Albino Rats (5/sex/group; except B1 had 4♀)	• Intravenous - group A; Oral by gavage - groups B, C & D • groups A1 & A2 injected w/1.0 mg/kg; groups B1 & B2 dosed w/10 mg/kg; groups C1 & C2 pretreated w/ 14 daily doses of unlabeled test material (meta isomer, 96.4% purity) followed by 10 mg/kg of labelled material; groups D1 & D2 dosed w/400 mg/kg of respective radiolabeled isomer • para (98% purity): 25.650 μCi/mg - groups A1, B1 & C1 or 2.75 μCi/mg - group D1; meta (99% purity): 28.545 μCi/mg - groups A2, B2 & C2 or 2.577 μCi/mg - group D2		**Absorption**: The fraction of the orally administered dose excreted within 24 hours of dosing ranged from 90 to 95%, indicating that the dose was rapidly absorbed in the gastrointestinal tract. There was no apparent sex-related difference in the uptake of the test material nor in the uptake of either isomer. **Distribution**: Residue levels of radiolabel with all dosing regimes were quite low 7 days after dosing with 0.04 to 0.34% of the administered dose recovered in the carcass. **Metabolism**: The predominant metabolite was the p- or m-toluic acid moieties which constituted from 50 to 60% of the administered dose. Other sites of metabolism included the a-hydroxylation of p- or m-toluic acid and the p- or m-toluic acid, methyl ester moieties and the further oxidation of these methyl groups to the carboxyl groups. There was no apparent sex-related difference in the metabolism of the test material nor were there any differences in the metabolism of either isomer or with any of the dosing regimes. **Excretion**: Approximately 80% of the administered dose was recovered in the urine. The fraction of the administered dose excreted within 24 hours of dosing ranged from 90 to 95%. The route of dosing or treatment with low- or high-dose levels did not alter the excretion profiles. There was no apparent sex-related difference in the excretion of the test material nor were any differences in the excretion of either isomer.
Acute Toxicity Studies			
AC 222,293 Technical			
Acute Oral - Charles River Rats (5/sex)	• 5000 mg/kg bw • purity N/S		**LD_{50} > 5000 mg/kg bw** (♂s & ♀s) 5000 mg/kg bw: ataxia, salivation, depression & prostration during the first 8 hrs postdosing, returning to normal by 24 hours postdosing, no mortalities. **Low Toxicity**

Study/Species/ # of Animals Per Group	Dose Levels/Purity of Test Material	NOAEL (mg/kg bw/day)	Results/Effects
Acute Oral - Charles River Mice (10♀/group)	• 1250, 2500 or 5000 mg/kg bw • purity N/S		**LD_{50} > 5000 mg/kg bw** (♀s) ≥2500 mg/kg bw: ataxia and prostration; 5000 mg/kg bw: 2 mortalities within 24 hours of dosing. **Low Toxicity**
Acute Dermal - New Zealand White Rabbits (5/sex)	• 2000 mg/kg bw to intact skin • purity N/S		**LD_{50} > 2000 mg/kg bw** (♂s & ♀s) No signs of treatment-related toxicity or mortalities. **Low Toxicity**
Acute Inhalation - Sprague-Dawley Rats (10/sex)	• 1.08 mg/L (gravimetric); 0.97 mg/L (analytical), 4-hr whole body exposure • 94.2% purity		**LC_{50} > 1.08 mg/L** (♂s & ♀s) No signs of treatment-related toxicity or mortalities. **Low Toxicity**
Dermal Irritation - New Zealand White Rabbits (6 rabbits, sex N/S)	• 0.5 g/intact & abraded skin sites • purity N/S		***Intact Skin Site***: 24 and 72 hours: scores for all animals were zero for both erythema and edema. ***Abraded Skin Site***: 24 and 72 hours: scores for all animals were zero for both erythema and edema. **Not a dermal irritant**
Eye Irritation - New Zealand White Rabbits (9 rabbits, sex N/S)	• 100 mg/eye, 3 animals had their treated eyes irrigated • purity N/S		***Irrigated Group***: no signs of irritation noted in any animal. ***Non-irrigatedGroup***: 24 hours: corneal opacity (4/6 animals) and conjunctival irritation (6/6 animals); 48 hours: corneal opacity (1/6 animals) and conjunctival irritation (3/6 animals); 72 hours: all scores for cornea, iris and conjunctivae were zero for all animals. **Slight Eye Irritant**
Dermal Sensitization - Hartley Guinea Pigs (10♂/group)	• 25% w/v in saline used for induction & challenge • Buehler method • 94.2% purity		Induction Phase: scores for all animals were zero for both erythema and edema. Challenge Phase: scores for all animals were zero for both erythema and edema. **Not a skin sensitizer**

Study/Species/ # of Animals Per Group	Dose Levels/Purity of Test Material	NOAEL (mg/kg bw/day)	Results/Effects
CL 239,589 para isomer of imazamethabenz-methyl			
Acute Oral - Charles River Rats (5/sex)	• 5000 mg/kg bw • purity 90%		**LD_{50} > 5000 mg/kg bw** (♂s & ♀s) 5000 mg/kg bw: ataxia, prostration & diuresis were noted during the first 24 hours, no mortalities. **Low Toxicity**
Acute Dermal - New Zealand White Rabbits (5/sex)	• 2000 mg/kg bw to intact skin • 90% purity		**LD_{50} > 2000 mg/kg bw** (♂s & ♀s) No mortalities, no signs of toxicity. **Low Toxicity**
Dermal Irritation - New Zealand White Rabbits (6 rabbits, sex N/S)	• 0.5 g/intact & abraded skin sites • purity 90%		***Intact Skin Site***: 24 and 72 hours: scores for all animals were zero for both erythema and edema. ***Abraded Skin Site***: 24 hours: very slight erythema (5/6 animals), no signs of edema in any rabbit; 72 hours: very slight erythema (1/6 animals), no signs of edema in any rabbit. **A primary irritation score of 0.29** **A very mild skin irritant**
Eye Irritation - New Zealand White Rabbits (6 rabbits, sex N/S)	• 100 mg/eye • 90% purity		1 hour: conjunctival irritation (6/6 animals); 24 hours: less severe conjunctival irritation (4/6 animals); 48 hours: no signs of irritation were noted. **A mild eye irritant**
CL 252,767 meta isomer of imazamethabenz-methyl			
Acute Oral - Charles River Rats (5/sex)	• 5000 mg/kg bw • 88% purity		**LD_{50} > 5000 mg/kg bw** (♂s & ♀s) No signs of toxicity or mortalities. **Low Toxicity**
Acute Dermal - New Zealand White Rabbits (5/sex)	• 2000 mg/kg bw to intact skin • 88% purity		**LD_{50} > 2000 mg/kg bw** (♂s & ♀s) No signs of toxicity or mortalities. **Low Toxicity**
Dermal Irritation - New Zealand White Rabbits	• 0.5 g/intact & abraded skin sites • 88% purity		***Intact Skin Site***: 24 and 72 hours: scores for all animals were zero for both erythema and edema.

Study/Species/ # of Animals Per Group	Dose Levels/Purity of Test Material	NOAEL (mg/kg bw/day)	Results/Effects
(6 rabbits, sex N/S)			***Abraded Skin Site***: 24 hours: slight erythema (6/6 animals), no signs of edema in any rabbit; 72 hours: no signs of erythema or edema in any rabbit. **A primary irritation score of 0.25** **A very mild skin irritant**
Eye Irritation - New Zealand White Rabbits (6 rabbits, sex N/S)	• 100 mg/eye • 88% purity		1 hour: conjunctival irritation (6/6 animals); 24 hours: less intense conjunctival irritation (2/6 animals); 48 hours: no signs of irritation were noted. **A mild eye irritant**
Short-term Toxicity Studies			
AC 222,293 Technical			
21-Day Dermal Toxicity - New Zealand White Rabbits (6/sex/group)	• 0, 50, 100 or 200 mg/kg bw/day to intact & abraded skin sites, 6 hours/ day, 5 days/week for 3 weeks • 94.2% purity	Systemic NOAEL = 200 Dermal irritation LOAEL = 50	≥50 mg/kg bw/day: slight to moderate erythema & edema, slight desquamation & slight to moderate fissuring, thickened skin with red and/or raised areas, superficial crusting, microabsces(es), epidermal hyperplasia and chronic dermatitis; ≥100 mg/kg bw/day: pustules.
13-Week Dietary Toxicity - Sprague Dawley Rats (30/sex/group, 10/sex/group sacrificed at days 44 to 45 for clinical chemistry)	• 0, 1000, 5000 or 10 000 ppm (≈0, 50, 250 or 500 mg/kg bw/day) • 91.9% purity	NOAEL = 50/500 (♂/♀)	≥250 mg/kg bw/day: ↓ bw, hypertrophy of hepatic cells (♂); 500 mg/kg bw/day: ↑ SGPT & SGOT, ↑ relative liver wts, intracytoplasmic "myelin figures" in hepatic cells (♂).
1-Year Dietary Toxicity - Beagle Dogs (8/sex/group)	• 0, 250, 1000 or 4000 ppm (≈0, 6.3, 25 or 100 mg/kg bw/day) • 94.2% purity	NOAEL = 25/100 (♂/♀)	100 mg/kg bw/day: ↓ Hgb, RBC and Hct; ↑ relative liver, spleen & heart wts, ↓ bw (♂). Effects on hematological parameters were noted at treatment weeks 13, 26 & 52.

Study/Species/ # of Animals Per Group	Dose Levels/Purity of Test Material	NOAEL (mg/kg bw/day)	Results/Effects
Chronic Toxicity/Oncogenicity Studies			
AC 222,293 Technical			
18-Month Dietary Toxicity - CD-1 Mice (65/sex/group, 10 mice sacrificed @ 12 months)	• 0, 130, 525 or 2100 ppm (= 0, 18.6, 75.1 or 300 mg/kg bw/day) • 94.2% purity	NOAEL = 75.1/18.6 (♂/♀)	≥75.1 mg/kg bw/day: ↑ relative thyroid/ parathyroid & adrenal wts (♀); 300 mg/kg bw/day: ↑ relative thyroid/parathyroid & adrenal wts (♂). **No evidence of carcinogenicity.**
2-Year Dietary Toxicity - Sprague Dawley Rats (65/sex/group, 10 rats sacrificed @ 12 months)	• 0, 250, 1000 or 4000 ppm (=0, 12.5, 50 or 200 mg/kg bw/day) • 94.2% purity	NOAEL = 12.5	≥50 mg/kg bw/day: ↑ SGOT & SGPT, ↑ SAP & GGT, ↑ incidence of hepatocellular degeneration (♂); ↓ bw & bwg (♀); 200 mg/kg bw/day: ↑ SGOT & SGPT; ↓ bw & bwg (♂); ↑ incidence of hepatocellular vacuolation and epithelial hyperplasia of the thymus (♀). **No evidence of carcinogenicity.**
Developmental/Reproductive Toxicity Studies			
AC 222,293 Technical			
Pilot Teratology Study, Oral - Sprague Dawley Rats (5♀/group)	• 0, 125, 250, 500 or 1000 mg/kg bw/day on gestation days 6 to 15 (by gavage, in corn oil) • 94.2% purity		**Maternal**: ≥125 mg/kg bw/day: ↑ incidence & degree of salivation following dosing; 1000 mg/kg bw/day: mottled kidney (1 dam).
Teratology Study, Oral - Sprague Dawley Rats (25♀/group)	• 0, 250, 500 or 1000 mg/kg bw/day on gestation days 6 to 15 (by gavage, in corn oil) • 94.2% purity	Maternal = 1000 Develop-mental = 1000	**Maternal**: ≥500 mg/kg bw/day: slightly ↑ incidence of salivation & pawing of the cage bottom (*not considered adverse*); 1000 mg/kg bw/day: moderately ↑ incidence of reddish-brown discharge around the mouth & nasal areas & dry-stained urogenital areas (*not considered adverse*). **Developmental**: 1000 mg/kg bw/day: thread-like tail & anal atresia (1 fetus: within historical controls), cleft palate with short lower jaw (1 fetus: 0% incidence in 3401 fetuses from 262 litters), absence of all caudal vertebrae (1 fetus which also displayed thread-like tail and anal atresia), absence of caudal vertebrae (3 fetuses appear to have delayed ossification) (*not considered adverse*). **No evidence of teratogenicity.**

Study/Species/ # of Animals Per Group	Dose Levels/Purity of Test Material	NOAEL (mg/kg bw/day)	Results/Effects
Range-finding Teratology Study, Oral - New Zealand White Rabbits (5♀/group)	• 0, 50, 150, 300, 650 or 1000 mg/kg bw/day on gestation days 6 to 18 (by gavage, in methyl cellulose) • 94.2% purity		**Maternal**: 1000 mg/kg bw/day: 4 mortalities between gestation days 8 and 26, ↓ bw (9.6 to 18.5% gestation days 12 to 24), ↓ urination & defecation prior to death, congested and edematous gastric epithelium, congested liver and biliary stasis.
Teratology Study, Oral - New Zealand White Rabbits (18♀/group)	• 0, 250, 500 or 750 mg/kg bw/day on gestation days 6 to 18 (by gavage, in methyl cellulose) • 94.2% purity	Maternal = 250 Develop-mental = 500	**Maternal**: >500 mg/kg bw/day: ↓ bwg. **Developmental**: 750 mg/kg bw/day: ↑ # of postimplantation losses/dam. **No evidence of teratogenicity.**
Dietary Reproduction Study - Sprague Dawley CD Rats 3-generation, 2 litters/generation (12♂ and 24♀/group)	• 0, 250, 1000 or 4000 ppm (= 0, 23.2/25.9, 91.9/ 103 or 374/406 mg/kg bw/day F_0 (♂/♀); 20.0/22.4, 82.8/93.2 or 329/358 mg/kg bw/day F_1 (♂/♀); 22.0/25.2, 87.2/ 101 or 353/392 mg/kg bw/day F_2 (♂/♀)) for 68 days pre-mating and from weaning to 100 days of age • 94.2% purity	Parental = 374/406 (♂/♀) Reproductive = 374/406 (♂/♀) Offspring = 374/406 (♂/♀)	**Parental**: No signs of treatment-related toxicity or mortalities. **Reproductive**: No signs of treatment-related toxicity or mortalities. **Offspring**: No signs of treatment-related toxicity or mortalities.
Genotoxicity Studies			
AC 222,293 Technical			
In vivo Dominant Lethal Assay - Charles River Rats (10♂/group)	• 0, 100, 300 or 1000 mg/kg bw for 5 days (by gavage) • 94.2% purity	> 300 mg/kg bw/day: salivation postdosing. **Negative**	
In vitro Chromosome Aberrations • CHO Cells	• 250, 500, 1000, 2000 or 4000 μg/mL ± activation • 94.2% purity	**Negative**	

Study/Species/ # of Animals Per Group	Dose Levels/Purity of Test Material	NOAEL (mg/kg bw/day)	Results/Effects
In vitro Unscheduled DNA Synthesis Studies • Primary Rat Hepatocyte Cultures	• 31.25, 62.5, 125, 250 or 500 µg/mL • 94.2% purity	**Negative**	
In vitro Gene Mutation Assay • CHO/HGPRT	• 10 to 5000 µg/ml • + activation; 1 to 1000 µg/mL - activation • 94.2% purity	**Negative**	
In vitro Reverse Mutation/Ames Assay • *Salmonella typhimurium* strains TA98, TA100, TA1535, TA1537 and TA1538	• Plate incorporation: 0, 50, 158, 500, 1581 or 5000 µg in DMSO, ± activation • 100% purity	**Negative**	
Toxicity Studies for Metabolites of Technical			
CL 263,840 [p-toluic acid, 2-(4-isopropyl-4-methyl-5-oxo-2-imidazolin-2-yl) & m-toluic acid, 6-(4-isopropyl-4-methyl-5-oxo-2-imidazolin-2-yl) (11:9)]			
Acute Oral - Charles River Rats (5/sex)	• 5000 mg/kg bw • 89.3% purity	**LD_{50} > 5000 mg/kg bw (♂s & ♀s)** 5000 mg/kg bw/day: diuresis in all animals; unilateral hydronephrosis (1/5♂s); liquid filled uterus (1/5♀s), no mortalities. **Low Toxicity**	
CL 119,610 [m-toluic acid, α-hydroxy-2-(4-isopropyl-4-methyl-5-oxo-2-imidazolin-2-yl)]			
Acute Oral - Charles River Rats (5/sex)	• 5000 mg/kg bw • >95% purity	**LD_{50} > 5000 mg/kg bw (♂s & ♀s)** 5000 mg/kg bw/day: diuresis in all animals, no mortalities. **Low Toxicity**	
CL 119,611 [m-toluic acid, α-hydroxy-6-(4-isopropyl-4-methyl-5-oxo-2-imidazolin-2-yl)-methyl ester]			
Acute Oral - Charles River Rats (5/sex)	• 5000 mg/kg bw • >95% purity	**LD_{50} > 5000 mg/kg bw (♂s & ♀s)** 5000 mg/kg bw/day: diuresis in all animals; liquid-filled uterus (1/5♀s), no mortalities. **Low Toxicity**	

Study/Species/ # of Animals Per Group	Dose Levels/Purity of Test Material	NOAEL (mg/kg bw/day)	Results/Effects
CL 119,543 [p-toluic acid, α-hydroxy-2-(4-isopropyl-4-methyl-5-oxo-2-imidazolin-2-yl)]			
Acute Oral - Charles River Rats (5/sex)	• 5000 mg/kg bw • purity N/S		**LD_{50} > 5000 mg/kg bw (♂s & ♀s)** 5000 mg/kg bw/day: diuresis in all animals 2 to 8 hours post treatment, recovery 24 hours post treatment, lung congestion (1/5♂s & 1/5♀s - ♀ that died), no mortalities (♂s); 1/5 mortalities (♀s). **Low Toxicity**
CL 119,544 [p-toluic acid, α-hydroxy-2-(4-isopropyl-4-methyl-5-oxo-2-imidazolin-2-yl)-methyl ester]			
Acute Oral - Charles River Rats (5/sex)	• 5000 mg/kg bw • > 95% purity		**LD_{50} > 5000 mg/kg bw (♂s & ♀s)** 5000 mg/kg bw/day: diuresis in all animals 2 to 8 hours posttreatment, recovery 24 hours posttreatment, no mortalities. **Low Toxicity**

Appendix IV Toxicology Endpoints for Use in Health Risk Assessment for Imazamethabenz-Methyl

Exposure Scenario	Endpoint	Study	Dose (mg/kg bw/day)	CAF or MOE[a]
Acute Dietary	Not required			
Chronic Dietary	↑ incidence of hepatocellular degeneration & alterations in hepatic enzyme levels in males, ↓ weight gain in females	An oral 2-year chronic dietary study in rats	12.5	100
	ADI = 0.125 mg/kg bw/day			
Short- and Intermediate-Term Dermal	No treatment related signs of systemic toxicity	A dermal 21-day toxicity study in rabbits	200 (highest dose tested)	100
Short- and Intermediate-Term Inhalation	↑ relative spleen, heart & liver weights, ↓ body weight (males), hematological effects	A 1-year dietary toxicity study in dogs	25	100
Aggregate Risk Assessment	Dermal component: no treatment related signs of systemic toxicity	A dermal 21-day toxicity study in rabbits	200 (highest dose tested)	100
	Inhalation[b] & Oral component (dietary & incidental): ↑ relative spleen, heart & liver weights, ↓ body weights & slight hematological effects	1-year dietary toxicity study in dogs	25	100

[a] Composite assessment factor (CAF) refers to total of uncertainty and *Pest Control Products Act* factors for dietary assessments, MOE refers to desired margin of exposure for occupational or non-occupational assessments.

[b] Given an oral NOAEL was selected, an inhalation absorption factor of 100% (default value) should be used in route-to-route extrapolation.

Appendix V Summary of Occupational Risk Estimates for Imazamethabenz-Methyl

Table 1 Route Specific MOEs for Mixers/Loaders and Applicators of Products containing Imazamethabenz-Methyl

Crop	Formulation Type[a]	Rate (kg a.i./ha)	Area Treated (ha/day)[b]	Target MOE = 100	
				Dermal MOE[c]	Inhalation MOE[d] Without Respirator
Groundboom: Baseline PPE (single layer with gloves for mixers/loaders); open M/L; open cab					
Spring wheat, durum wheat, spring barley and annual ryegrass	Liquid	0.48	100	3467	14 242
			300	1156	4747
Spring wheat, durum wheat and spring barley	Soluble granules	0.5	100	1423	17 677
			300	474	5892
Sunflowers	Liquid	0.25	100	6527	26 808
			300	2175	8936
	Soluble granules	0.25	100	2846	35 354
			300	949	11 785

[a] In the PHED tables, the term used for soluble granules is dry flowables.

[b] Area treated per day based on default values.

[c] Dermal MOE = NOAEL/ dermal exposure. The NOAEL for short-term and intermediate-term exposure is 200 mg/kg bw/day from a dermal study. Dermal exposure is calculated using the use rate (kg a.i./ha) × area treated per day (ha/day) × dermal unit exposure value (µg a.i./kg a.i. handled) divided by body weight (70 kg).

[d] Inhalation MOE = NOAEL/inhalation exposure. The NOAEL for short-term and intermediate-term inhalation exposure is 25 mg/kg bw/day from an oral study. Inhalation exposure is calculated using the use rate (kg a.i./ha) × area treated per day (ha/day) × inhalation unit exposure value (µg a.i./kg a.i. handled) divided by body weight (70 kg).

Table 2 Postapplication Exposure Estimates for Re-entry into Fields Treated with Imazamethabenz-Methyl

Activity	Crop Height/ Foliage Development	Transfer Coefficient (cm^2/hr)	Rate (kg a.i./ha)	MOE[a] (Day 0)	Proposed REI[b]	Safe Residue Limit (SRL)[c]
Workers in Cereal Field[d]						**Target MOE : 100**
Scouting	Low/Full	1500	0.5	1 167	0	11.67
	Low/Min	100		17 500	0	175
Workers in Sunflower Fields						**Target MOE: 100**
Scouting	High/Full	1000	0.25	3 431	0	17.5
	Low/Min	400		8 578	0	43.75
	High/Min	400		8 578	0	43.75

[a] Based on short-term dermal NOAEL of 200 mg/kg bw/day and target MOE of 100.

[b] REI= Restricted-entry interval

[c] $\text{SRL } (\mu g/cm^2) = \frac{\text{NOAEL } (\mu g/kg) \times \text{bw (kg)}}{\text{TC } (cm^2/hr) \times \text{Duration (hrs)} \times \text{Target MOE (unitless)}}$

[d] Cereal = Spring wheat, durum wheat, spring barley, barley and annual ryegrass

Appendix VI Dietary Exposure and Risk Estimates for Imazamethabenz-Methyl

Aggregate Dietary (Food and Water) Exposure and Risk Estimates for Imazamethabenz-Methyl

Imazamethabenz-Methyl		
	Chronic	
	ADI = 0.125 mg/kg bw/day	
Population	**Exposure (mg/kg bw/day)**	**%ADI**
Canadian population	0.007115	6
All infants (<1 year)	0.02284	18
Children 1 to 2 yrs	0.010701	9
Nursing infants	0.008482	7
Non nursing infants	0.028288	23
Children 3 to 5 yrs	0.010052	8
Children 6 to 12 yrs	0.00694	6
Youth 13 to 19 yrs	0.005189	4
Adults 20 to 49 yrs	0.006629	5
Adults 50+ yrs	0.006935	6
Females 13 to 49 yrs	0.006586	5

Appendix VII Residue Chemistry Summary for Imazamethabenz-Methyl

1.1 Metabolism

The PMRA concluded that the residue chemistry database for imazamethabenz-methyl is complete. Nature and magnitude of the residue in plants and livestock are adequately understood. Conclusions from the United States Environmental Protection Agency are consistent with the PMRA's conclusions.

1.1.1 Plant Metabolism

In wheat, barley and sunflower, imazamethabenz-methyl is rapidly and efficiently absorbed through the roots and foliage of plants and is highly xylem mobile. The herbicidally active imazamethabenz-methyl acid (in the ester form of the parent molecule) is mobile in the phloem. The acid is produced in appreciable amounts only in susceptible weeds and accumulates in the meristematic regions. Imazamethabenz-methyl acid kills plants by inhibiting acetohydroxyacid synthase, which is involved in the biosynthesis of branched chain amino acids valine, leucine and isoleucine. This causes a disruption of protein which in turn leads to an interference in DNA synthesis and cell growth. It is also noted that the mechanism of selectivity of imazamethabenz-methyl in tolerant plants is due to the oxidation of the aryl methyl moiety to the corresponding hydroxymethyl derivative, followed by carbohydrate conjugation. Both of these steps result in loss of herbicidal activity. Susceptible plants primarily hydrolyse the imazamethabenz-methyl ester, producing the phytotoxic imazamethabenz-methyl acid.

The PMRA has concluded that the qualitative nature of imazamethabenz-methyl residues in plants is understood based on studies conducted on wheat and sunflower. Due to its acetolactate synthase inhibitor properties, imazamethabenz-methyl is used to control wild oat and other weeds in wheat and barley. Selectivity is based on different metabolism rates between the crops and susceptible species. The meta isomer is more phytotoxic to wild oat than the para isomer. In wheat, hydroxylation of the methyl group of the benzene ring appears to be the major metabolic pathway, followed by glucoside conjugation. Other metabolites identified are its free acid and its aryl methyl hydroxylated alcohol as well as its carbohydrate conjugates. Data indicate that the meta-isomer is more rapidly metabolised than thev *p*-isomer.

The USEPA has reviewed a sunflower metabolism study in which plants were treated once with either the para or meta isomer of ^{14}C-carboxyl imazamethabenz-methyl at 0.56 kg a.i./ha (two times the maximum rate) at the 6 to 8 leaf stage. Heads were harvested at maturity and separated in whole seeds. The total radioactive residue in whole seeds was less than 0.01 ppm.

1.1.2 Livestock Metabolism

The PMRA has on file a review of the metabolism of imazamethabenz-methyl in ruminants (cattle and goat) as well as on poultry. In the cattle metabolism study, collected samples of milk and tissues, including muscle, kidney, fat and liver showed no detectable ^{14}C residues (<0.01 ppm in milk and <0.05 ppm in tissue). In the goat metabolism studies, animals fed with a mixture of para and meta radiolabelled ^{14}C imazamethabenz-methyl showed no detectable residues in muscle, fat and blood. However, low levels of radioactivity were reported in milk

samples and quantifiable radioactive residues were detected in liver (0.08 ppm and 0.13 ppm) and kidney (0.44 ppm and 0.51 ppm).

In the poultry metabolism study, animals fed with a mixture of para and meta radiolabelled ^{14}C imazamethabenz-methyl showed no detectable residues in any tissue, blood and egg yolks and egg white samples (<0.05 ppm).

1.1.3 Residue Definition

Based on metabolism studies conducted on wheat and sunflower and the structural similarities between the para and meta isomers of parent methyl ester and acid metabolites, the PMRA has determined that the residues of concern for MRL enforcement as well as risk assessment should include the para and meta isomers of the parent methyl ester as well as their respective acid metabolites 6-(4-isopropyl-4-methyl-5-oxo-2-imidazolin-2-yl)-*m*-toluic acid and 2-(4-isopropyl-4-methyl-5-oxo-2-imidazolin-2-yl)-*p*-toluic acid.

Given livestock metabolism studies conducted at exaggerated dose rates showed no significant concentrations of imazamethabenz-methyl or its metabolites in meat, milk, poultry and egg; and since no significant residues are expected to be present in products intended for livestock consumption, the PMRA has concluded that there is no need to propose a residue definition for food of animal origin.

1.2 Analytical Methods

1.2.1 Methods for Residue Analysis of Plants and Plant Products

The PMRA has reviewed analytical methodology capable of determining residues of imazamethabenz-methyl and its metabolites in barley and wheat (grain and straw) as well as sunflower seeds. Para and meta isomers of toluic acid and methyl ester residues of imazamethabenz-methyl are analysed by gas chromatography using nitrogen-phosphorus detector. Sensitivity reported for barley and wheat (grain and straw) was 0.10 ppm and for sunflower seeds was 0.05 ppm.

1.2.2 Methods for Residue Analysis of Food of Animal Origin

Based on previous reviews, the PMRA considers the analytical method (M-1794) for determining residues of the parent compound and parent acid in cow's milk to be satisfactory.

1.2.3 Multiresidue Analytical Methods

Imazamethabenz-methyl is not listed in the Canadian Food Inspection Agency's multiresidue analytical methods manual (Volume 7).

1.3 Food Residues

1.3.1 Storage Stability

1.3.1.1 Storage Stability Data – Plants

The PMRA has determined that residues of imazamethabenz-methyl remain stable for at least 11 months when samples of wheat grain and straw are stored between -23°C and -29°C.

1.3.2 Crop Residues

The PMRA has reviewed barley, wheat and sunflower residue studies conducted in Manitoba, Saskatchewan and Alberta. When barley and wheat were treated at 0.6, 1.2 and 1.6 kg a.i./ha (registered rate is 0.6 kg a.i./ha), residues were all below the sensitivity of analytical methods M-1226 and M-1531. In barley straw, residues were found up to 1.87 ppm at 1.2 kg a.i./ha (report C-2604). In wheat straw, residues were found up to 0.91 ppm at 1.2 kg a.i./ha (report C-2543). No residues were detected in sunflower seeds at either application rate (0.4 and 1.12 kg a.i./ha).

1.3.3 Livestock Residues

No residues were detected in collected samples of milk and tissues, including muscle, kidney, fat and liver, of cattle fed with 2 ppm ^{14}C mixture of meta and para imazamethabenz-methyl for seven days.

However, the need for an additional cattle feeding study is reserved pending a review of residue data on hay and forage. Based on the current registered uses, no finite residues are expected.

Based on the Canadian MRL for barley grain, wheat grain and sunflower as well as American tolerances for barley straw and wheat straw, the maximum theoretical dietary burden (MTDB) for dairy cattle is 0.56 ppm for the combined residues of imazamethabenz-methyl and its acid metabolites.

In the goat metabolism studies, levels of radioactivity were reported in milk samples (0.012–0.017 ppm) and quantifiable radioactive residues were detected in liver (0.08 ppm and 0.13 ppm) and kidney (0.44 ppm and 0.51 ppm) samples when animals were fed with a ^{14}C mixture of meta and para imazamethabenz-methyl at 7.5 ppm (14-fold the MTDB). Based on good agricultural practices, the magnitude of residue should be:

- 0.0012 ppm in milk;
- 0.0094 ppm in liver; and
- 0.0368 ppm in kidney.

Based on the Canadian MRL for barley grain and sunflower, the maximum theoretical dietary burden (MTDB) for poultry is 0.1 ppm for the combined residues of imazamethabenz-methyl and its acid metabolites. In the poultry metabolism study, animals fed with a mixture of 1.2 ppm para and meta radiolabelled ^{14}C imazamethabenz-methyl showed no detectable residues in any tissue, blood or egg yolks and white samples. Based on the current registered uses, no finite residues are expected.

1.3.4 Confined Accumulation in Rotational Crops

The PMRA has reviewed the uptake and residual radioactivity in green bean, sweet corn and radish planted four weeks and six weeks after treatment of the soil at an application rate of 0.8 kg a.i./ha with either the para and meta isomer of ^{14}C labelled imazamethabenz-methyl. Data for green bean foliage suggest that there is the potential for quantifiable residues in leafy vegetables which may be planted in rotation to crops. Analysis of the para and meta isomers showed that the major metabolites were hydroxymethyl metabolites, accounting for 25% and 55% of the TRR (total radioactive residues) respectively. Minor amounts of their acid metabolites were also characterized, accounting for 8% and 9% of the TRR respectively.

The PMRA has on file the conclusions of another confined study in which spring wheat, lettuce and carrots were planted in soil treated with imazamethabenz methyl at a rate of 0.84 kg a.i./ha. The only crop to survive was the winter wheat, planted 92 days after treatment. For the para isomer, total radioactive residue(s) (TRR) levels were 0.05 ppm in forage, 0.01 ppm in heads and 0.02 ppm in straw. For the meta isomer, TRR levels were 0.05 ppm in forage and 0.01 ppm in heads and straw.

1.3.5 Processed Food

Processing studies for sunflower seeds and cereal grains were not carried out as residues were not detected in crops treated at exaggerated rates.

Appendix VIII Environmental Fate and Toxicity

Table 1 Environmental Fate of Imazamethabenz-Methyl (ASS) and its Transformation Products

Study Type	Test Material	Study Conditions	Value or Endpoint	Interpretation	Major Transformation Products
Abiotic transformation					
Hydrolysis	ASS Combined ester	pH 5 pH 7 pH 7.05 pH 9	$t_{1/2}$ (day) = 322 $t_{1/2}$ (day) = 75 $t_{1/2}$ (day) = 119 $t_{1/2}$ (day) = 1.11	Persistent Moderately persistent Moderately persistent Non-persistent	Meta and para acid and amides
	ASS Meta ester	15°C pH 5 pH 7 pH 9 25°C pH 5 pH 6 pH 7 pH 8 pH 9 35°C pH 5 pH 7 pH 9	$t_{1/2}$ (day) = 730 $t_{1/2}$ (day) = 240 $t_{1/2}$ (day) = 3.5 $t_{1/2}$ (day) = 267 $t_{1/2}$ (day) = 220 $t_{1/2}$ (day) = 60–63 $t_{1/2}$ (day) = 10 $t_{1/2}$ (day) = 0.9–1.0 $t_{1/2}$ (day) = 94 $t_{1/2}$ (day) = 16 $t_{1/2}$ (day) = 0.4	Not a major route of transformation at acidic and neutral conditions especially between 15 and 25	Meta acid and amides
	ASS Para ester	15°C pH 5 pH 7 pH 9 25°C pH 5 pH 6 pH 7 pH 8 pH 9 35°C pH 5 pH 7 pH 9	$t_{1/2}$ (day) = 1340 $t_{1/2}$ (day) = 420 $t_{1/2}$ (day) = 6.2 $t_{1/2}$ (day) = 295–500 $t_{1/2}$ (day) = 430 $t_{1/2}$ (day) = 98–115 $t_{1/2}$ (day) = 16 $t_{1/2}$ (day) = 1.5–1.7 $t_{1/2}$ (day) = 185 $t_{1/2}$ (day) = 28 $t_{1/2}$ (day) = 0.5	Not a major route of transformation at acidic and neutral conditions especially between 15 and 25°C	Para acid and amides
Phototransformation soil	ASS Meta ester	Princeton sandy loam; 28 d–25°C	$t_{1/2}$ (day) = 53	Not a major route of transformation	None
	ASS Para ester	Princeton sandy loam; 28 d–25°C	$t_{1/2}$ (day) = 73		

Study Type	Test Material	Study Conditions	Value or Endpoint	Interpretation	Major Transformation Products
Phototrans-formation water	ASS Combined ester	pH 5 (25°C) pH 7 (25°C) pH 9 (25°C) Drinking water Pure water, 50° Latitude, Spring	$t_{1/2}$ (day) = 21.4–22.8 $t_{1/2}$ (day) = 14.5–14.9 $t_{1/2}$ (day) = 7.1–7.2 $t_{1/2}$ (day) = 14.8–15.2 $t_{1/2}$ (day) = 10.4	Not a major route of transformation in acidic and neutral environment	CL 119,681 and CL 119,682
	ASS Meta ester	pH 5 (25°C) pH 7 (25°C) (19°C) (19°C dark control) pH 9 (25°C) Pond water Pure water, 50° Latitude, Spring	$t_{1/2}$ (day) = 27–50.2 $t_{1/2}$ (day) = 3.6 $t_{1/2}$ (day) = 0.3 $t_{1/2}$ (day) = 24.1 $t_{1/2}$ (day) = 8.7 $t_{1/2}$ (day) = 31.4 $t_{1/2}$ (day) = 9.6	Not a major route of transformation in acidic and neutral environment, especially at 25°C	CL 119,681
	ASS Para ester	pH 5 (25°C) pH 7 (25°C) (19°C) (19°C dark control) pH 9 (25°C) Pond water Pure water, 50° Latitude, Spring	$t_{1/2}$ (day) = 25.1–36 $t_{1/2}$ (day) = 20 $t_{1/2}$ (day) = 0.5 $t_{1/2}$ (day) = 96.3 $t_{1/2}$ (day) = 10 $t_{1/2}$ (day) = 19.4 $t_{1/2}$ (day) = 11.2	Not a major route of transformation in acidic and neutral environment, especially at 25°C	CL 119,682
	Meta acid	pH 5 (25°C) pH 7 (25°C) pH 9 (25°C)	$t_{1/2}$ (day) = 0.5 $t_{1/2}$ (day) = 0.5 $t_{1/2}$ (day) = 0.4	A major route of transformation in the environment	4-methyl, 2-carboxybenzaldehyde 4-methyl phthalic acid 3-hydroxy-5-(or 4-) methyl-phthalimidine 5-methylphthalimide 4-methyl-phthalamide
	Para acid	pH 5 (25°C) pH 7 (25°C) pH 9 (25°C)	$t_{1/2}$ (day) = 0.7 $t_{1/2}$ (day) = 0.6 $t_{1/2}$ (day) = 0.6	A major route of transformation in the environment	5-methyl, 2-carboxybenzaldehyde 4-methyl phthalic acid 3-hydroxy-5-(or 4-) methyl-phthalimidine 5-methylphthalimide 4-methyl-phthalamide

Study Type	Test Material	Study Conditions	Value or Endpoint	Interpretation	Major Transformation Products
Biotransformation					
Soil–aerobic	ASS Combined esters	Haguenau silt loam, pH 6.5, OM 1.5% Manzanilla sdy loam pH 8.2, OM 1.1 Nierstein silt loam, pH 7.9, OM 5% Saint-Paul-le-Roman sdy loam, pH 6.9, OM 1.8%	$t_{1/2}$ (day) = 74 $t_{1/2}$ (day) = 125 $t_{1/2}$ (day) = 48 $t_{1/2}$ (day) = 67	Moderately persistent Moderately persistent Moderately persistent Moderately persistent	
	ASS Meta ester	Princeton sdy loam, pH 4.8, OM 0.9% and 22°C North Dakota cl loam, pH 7.6, OM 4.6% and 22°C Sion Hill sdy loam, pH 4, OM 2.7%, moisture 40%, 21°C Riverside cl loam, pH 5.8, OM 6.6, moisture 40%, 21°C	$t_{1/2}$ (day) = 234 $t_{1/2}$ (day) = 207 DT_{50} (day) = 19.6 DT_{50} (day) = 16.1	Persistent Persistent Slightly persistent Slightly persistent	
	ASS Para ester	Princeton sdy loam, pH 4.8, OM 0.9% and 22°C North Dakota cl loam, pH 7.6, OM 4.6% and 22°C Sion Hill sdy loam, pH 4, OM 2.7%, moisture 40%, 21°C Riverside cl loam, pH 5.8, OM 6.6, moisture 40%, 21°C	$t_{1/2}$ (day) = 195 $t_{1/2}$ (day) = 129 DT_{50} (day) = 14.7 DT_{50} (day) = 10.5	Persistent Moderately persistent Non-persistent Non-persistent	

Study Type	Test Material	Study Conditions	Value or Endpoint	Interpretation	Major Transformation Products
	ASS Acid	Nierstein silt loam, pH 7.9, OM 5% St-Paul Le Roman sdy loam, pH 6.9, OM 1.8% Sion Hill sdy loam, pH 4, OM 2.7%, moisture 40%, 21°C Riverside cl loam, pH 5.8, OM 6.6, moisture 40%, 21°C	$t_{1/2}$ (day) = 31 $t_{1/2}$ (day) = 51 DT_{50} (day) = 119 DT_{50} (day) = 46.2–60.2	Slightly peristent Moderately persistent Moderately persistent Slightly persistent	
Soil–anaerobic	ASS Meta ester	Princeton sdy loam, pH 4.8, OM 0.9% and 22°C	$t_{1/2}$ (day) = 195-234	Persistent	Meta acid and amides
	ASS Para ester	Princeton sdy loam, pH 4.8, OM 0.9% and 22°C	$t_{1/2}$ (day) = 195-234	Persistent	Para acid and amides
Water/ sediment–aerobic	ASS Meta ester	Delft ditch clay, Netherland, pH 7.1 River Kromme Rijn sdy loam, Netherland, pH 7.3 Pond water	$t_{1/2}$ (day) <7 $t_{1/2}$ (day) <7 $t_{1/2}$ (day) = 93–98	Non-persistent Non-persistent Moderately persistent	Three unknown transformation products
	ASS Para ester	Delft ditch clay, Netherland, pH 7.1 River Kromme Rijn sdy loam, Netherland, pH 7.3 Pond water	$t_{1/2}$ (day) <7 $t_{1/2}$ (day) <7 $t_{1/2}$ (day) = 137–160	Non-persistent Non-persistent Moderately persistent	Three unknown transformation products
	ASS Acid	Delft ditch clay, Netherland, pH 7.1 River Kromme Rijn sdy loam, Netherland, pH 7.3	$t_{1/2}$ (day) = 5.4 $t_{1/2}$ (day) = 3.1	Non-persistent Non-persistent	Not determined
	CL 119,681	Pond water: initial pH 6.9 and Sassafras sandy loam (New Jersey) of pH 6.9 and 1.0% OM	$t_{1/2}$ (day) < 3	Non-persistent	Not determined

Study Type	Test Material	Study Conditions	Value or Endpoint	Interpretation	Major Transformation Products
	CL 119,682	Pond water: initial pH 7.1 and Sassafras sandy loam (New Jersey) of pH 6.9 and 1.0% OM	$t_{1/2}$ (day) = 18.7	Slightly persistent	Not determined
Mobility					
Adsorption/ desorption	ASS Meta ester	Alberta silt loam, pH 5.4, OM 12.1% Manitoba sandy loam, pH 6.2, OM 3.3% Saskatchewan silt loam, pH 5.5, OM 5.8% Princeton sandy loam, pH 6.5, OM 2.1% Wisconsin silt loam, pH 6.3, OM 4.6%	K_{oc} = 150 K_{oc} = 86 K_{oc} = 93 K_{oc} = 26.3 K_{oc} = 25.1	Highly mobile Highly mobile Highly mobile Very highly mobile Very highly mobile	Not determined
	ASS Para ester	Alberta silt loam, pH 5.4, OM 12.1% Manitoba sandy loam, pH 6.2, OM 3.3% Saskatchewan silt loam, pH 5.5, OM 5.8% Princeton sandy loam, pH 6.5, OM 2.1% Wisconsin silt loam, pH 6.3, OM 4.6%	K_{oc} = 121 K_{oc} = 75 K_{oc} = 95 K_{oc} = 14.8 K_{oc} = 20.2	Highly mobile Highly mobile Highly mobile Very highly mobile Very highly mobile	Not determined
	ASS Meta acid	Sassafras sandy loam, pH 6.9, OM 1% Bluelah loamy sand, pH 6.5, OM 0.5% Beardon clay loam, pH 7.7, OM 5% Tippeecanoe silt loam, pH 5.2, OM 3%	K_{oc} = 5.2 K_{oc} = 13.5 K_{oc} = 4.1 K_{oc} = 17.1	Very highly mobile Very highly mobile Very highly mobile Very highly mobile	Not determined

Study Type	Test Material	Study Conditions	Value or Endpoint	Interpretation	Major Transformation Products
	ASS Para acid	Sassafras sandy loam, pH 6.9, OM 1% Bluelah loamy sand, pH 6.5, OM 0.5% Beardon clay loam, pH 7.7, OM 5% Tippeecanoe silt loam, pH 5.2, OM 3%	K_{oc} = 6.9 K_{oc} = 23.1 K_{oc} = 8 K_{oc} = 20.8	Very highly mobile Very highly mobile Very highly mobile Very highly mobile	Not determined
Soil column leaching	ASS combined ester	Princeton sandy loam, pH 6.5, OM 2.2% North Dakota clay loam, pH 7.6, OM 4.6%	Leachates = 34% AR with 77% as ASS Leachates < 12% AR with 95% as acid	Moderately mobile Low mobility	The meta and para acid

Study Type	Test Material	Study Conditions	Value or Endpoint	Interpretation	Major Transformation Products
Field studies					
Field dissipation	ASS	Canadian studies Vanscoy, Saskatchewan, sandy loam, OM 2.5% Ellerslie, Alberta, Silty clay loam, OM 11% Nova Scotia, Sandy loam US studies North Dakota, Sandy loam California Loamy sand Chico, California, Clay soil Hanford, California, Sandy loam Mont-Angel, California, Silt loam	DT_{50} (day) = 137 DT_{50} (day) = 70 DT_{50} (day) = 21–28 DT_{50} (day) = 47–60 DT_{50} (day) = 14 DT_{50} (day) = 118 DT_{50} (day) = 136 DT_{50} (day) = 202	Moderately persistent Moderately persistent Slightly persistent Moderately persistent Slightly persistent Moderately persistent Moderately persistent Persistent	The para and meta acid
Bioaccumulation	ASS Meta ester	Lipid solubility	K_{ow} = 35	Low potential for bioaccumulation	Not applicable
	ASS Para ester	Lipid solubility	K_{ow} = 66		
Bioconcentration	ASS Combined ester	Flow-through 44-day study with the bluegill sunfish *Lepomis macrochirus*) (fillet, whole fish, viscera)	BCF < 1.7 whole fish	bioconcentration is low	Not applicable

Table 2 Environmental Toxicity of Imazamethabenz-Methyl and Its Transformation Products

Organism	Study Type		Species	Test Material	Endpoint	Value (effect)	Effect of Concern
Terrestrial Species							
Invertebrate	Acute contact		Honey bee (*Apis mellifera*)	Technical	96–hrs LD_{50}	> 100 µg a.i./bee	Mortality
			Earthworm (*Eisenia foetida*)		14–day LD_{50}	> 20.8 mg a.i./kg soil	Mortality
Birds	Acute oral		Bobwhite quail (*Colinus virginianus*)	Technical	LD_{50}	>2150 mg a.i./kg bw	Mortality
			Mallard duck (*Anas platyrhynchos*)			>2150 mg a.i./kg bw	
	Dietary		Bobwhite quail (*Colinus virginianus*)	Technical	LC_{50}	>5000 mg a.i./kg diet	Mortality
			Mallard duck (*Anas platyrhynchos*)			>5000 mg a.i./kg diet	
	Reproduction		Bobwhite quail (*Colinus virginianus*)	Technical	NOEC	2000 mg a.i./kg diet	
			Mallard duck (*Anas platyrhynchos*)			2000 mg a.i./kg diet	
Mammals	Acute	Oral	Rat	Technical	LD_{50}	>5000 mg a.i./kg bw	Mortality
			Mouse		LD_{50}	>5000 mg a.i./kg bw	
			Rat	ASSERT 300 LC	LD_{50}	2333–3078 mg a.i./kg bw	
			Rat	Acid	LD_{50}	>5000 mg a.i./kg bw	

Organism	Study Type		Species	Test Material	Endpoint	Value (effect)	Effect of Concern
	Subchronic	Dietary 90-days	Rat	Technical	NOEL	87.5 mg a.i./kg bw	Mortality
	Chronic	3-generation reproduction	Rat	Technical	NOEC	250 mg a.i./kg diet	Reduced body weight
Terrestrial plants	Vegetative vigor		Black nightshade (*Solanum nigra*) dicotyledon	ASSERT 300 LC	EC^{25}	0.023 kg a.i./ha	Reduced size, vigor, stand
Freshwater Organisms							
Invertebrate	Acute		*Daphnia magna*	Technical	48-hrs LC_{50} NOEC	>100 mg a.i./L 100 mg a.i./L	Immobility
	Chronic		*Daphnia magna*	Technical	NOEC	> 8.5 mg a.i./L	Number of offspring per adult/ reproduction
Fish	Acute		Rainbow trout (*Oncorhynchus mykiss*)	Technical	96-hrs LC_{50} NOEC	>100 mg a.i./L 100 mg a.i./L	Mortality
			Bluegill sunfish (*Lepomis macrochirus*)		7-day LC_{50} NOEC	> 8.4 mg a.i./L 8.4 mg a.i./L	Mortality
	Chronic (Early Life Stage)		Fathead minnow (*Pimephales promelas*)	Technical	NOEC	< 0.32 mg a.i./L	Egg hatch-ability, survival of fry
Algae	Acute		*Selenastrum capricornutum*	Technical	72-hrs EC_{50} NOEC	100 mg a.i./L 49 mg a.i./L	Area under the growth curve and biomass
	Acute		*Anabaena flos-aquae*	Technical	96-hrs EC_{50} NOEC	26.9 mg a.i./L 5.7 mg a.i./L	Biomass

Organism	Study Type	Species	Test Material	Endpoint	Value (effect)	Effect of Concern
Aquatic vascular plants	Acute	Duckweed (*Lemna minor and Lemna gibba*) Immersed plant	Technical	7-day EC_{50} NOEC	0.0727 mg a.i./L <0.0105 mg a.i./L	Biomass, specific growth rate
		Transplanted rice (*Oriza sativa*) emerged plant	Technical	EC_{25}	0.146 kg a.i./ha	Reduced size, vigor, stand

Table 3 Summary of Screening Level Risk Assessment of Imazamethabenz-Methyl to Terrestrial Invertebrates and Plants

Organism	Exposure	Endpoint Reported	Use Rate (g a.i./ha)	EEC	RQ	Exceedance of LOC
Invertebrates						
Honeybee	Acute contact	LD_{50} > 100 µg a.i./bee (112 kg a.i./ha)	500	0.5 kg a.i./ha	4.5×10^{-4}	0
Earthworm		LC_{50} > 20.8 mg a.i./kg soil	500	2.22×10^{-2} mg a.i./kg soil	1.2×10^{-2}	0
Plants						
Plants	Vegetative vigor Black nightshade (*Solanum nigra*)	EC_{25} = 0.023 kg a.i./ha	250	0.255 kg a.i./ha	11.1	11.1-fold
	Transplanted rice* (*Oriza sativa*) emerged plant	EC_{25} = 0.146 kg a.i./ha	250	0.255 kg a.i./ha	1.7	1.7-fold

* Rice is known to grow mainly in aquatic environments, but is treated in risk characterization as a terrestrial plant due to its emerged plant parts.

Table 4 Summary of Screening Level Risk Assessment of Imazamethabenz-Methyl to Birds and Mammals

Organism	Exposure	Endpoint* (mg a.i./kg bw/day)	Food Guild	EDE (mg a.i./kg bw/day)	RQ	Exceedance of LOC
Birds						
Small (20 g)	Acute Oral	215	Insectivore	25.19	1.17×10^{-1}	0
			Granivore	4.34	2.0×10^{-2}	0
			Fructivore	12.75	5.9×10^{-2}	0
	Dietary	28.3	Insectivore	25.19	8.9×10^{-1}	0
			Granivore	4.34	15.3×10^{-2}	0
			Fructivore	12.75	4.5×10^{-1}	0
	Reproduction	113.1	Insectivore	25.19	2.2×10^{-1}	0
			Granivore	4.34	3.8×10^{-2}	0
			Fructivore	12.75	1.1×10^{-1}	0
Medium (100 g)	Acute Oral	215	Insectivore	19.66	9.1×10^{-2}	0
			Granivore	3.38	1.6×10^{-2}	0
			Fructivore	9.95	4.6×10^{-2}	0
	Dietary	28.3	Insectivore	19.66	6.9×10^{-1}	0
			Granivore	3.38	1.2×10^{-1}	0
			Fructivore	9.95	3.5×10^{-1}	0
	Reproduction	113.1	Insectivore	19.66	1.7×10^{-1}	0
			Granivore	3.38	3.0×10^{-2}	0
			Fructivore	9.95	8.8×10^{-2}	0

Organism	Exposure	Endpoint* (mg a.i./kg bw/day)	Food Guild	EDE (mg a.i./kg bw/day)	RQ	Exceedance of LOC
Large (1000 g)	Acute	215	Insectivore	5.74	1.2×10^{-3}	0
			Granivore	0.99	4.6×10^{-3}	0
			Fructivore	2.91	1.4×10^{-2}	0
			Herbivore	35.79	1.7×10^{-1}	0
	Dietary	28.3	Insectivore	5.74	2.0×10^{-1}	0
			Herbivore	0.99	3.5×10^{-2}	0
			Fructivore	2.91	1.0×10^{-1}	0
			Herbivore (Leaves and leafy crops)	35.79	1.26	1.26-fold
			Herbivore (short range grass)	20.5	7.2×10^{-1}	0
			Herbivore (long grass)	12.5	4.4×10^{-1}	0
			Herbivore (forage crops)	18.8	6.0×10^{-1}	0
	Reproduction	113.1	Insectivore	5.74	5.1×10^{-2}	0
			Granivore	0.99	8.6×10^{-3}	0
			Fructivore	2.91	2.6×10^{-2}	0
			Herbivore	35.79	3.2×10^{-1}	0
Mammals						
Small (15 g)	Acute Oral	233	Insectivore	14.5	6.2×10^{-2}	0
			Granivore	2.5	1.1×10^{-2}	0
			Fructivore	7.3	3.1×10^{-2}	0
			Herbivore	90.3	3.9×10^{-1}	0

Organism	Exposure	Endpoint* (mg a.i./kg bw/day)	Food Guild	EDE (mg a.i./kg bw/day)	RQ	Exceedance of LOC
	Subchronic	87.5	Insectivore	14.5	1.7×10^{-1}	0
			Granivore	2.5	2.9×10^{-2}	0
			Fructivore	7.3	8.3×10^{-2}	0
			Herbivore (Leaves and leafy crops)	90.3	1.03	1.03-fold
			Herbivore (short range grass)	51.8	5.9×10^{-1}	0
			Herbivore (long grass)	31.5	3.6×10^{-1}	0
			Herbivore (forage crops)	47.5	5.4×10^{-1}	0
Medium (35 g)	Acute Oral	233	Insectivore	12.4	5.3×10^{-2}	0
			Granivore	2.1	9.0×10^{-3}	0
			Fructivore	6.3	2.7×10^{-2}	0
			Herbivore	77.4	3.3×10^{-1}	0
	Subchronic	87.5	Insectivore	12.4	1.4×10^{-1}	0
			Granivore	2.1	2.4×10^{-2}	0
			Fructivore	6.3	7.2×10^{-2}	0
			Herbivore	77.4	8.8×10^{-1}	0
Large (1000 g)	Acute Oral	233	Insectivore	6.8	2.9×10^{-2}	0
			Granivore	1.2	5.2×10^{-3}	0
			Fructivore	3.4	1.5×10^{-2}	0
			Herbivore	42.3	1.8×10^{-1}	0
	Subchronic	87.5	Insectivore	6.8	7.8×10^{-2}	0
			Granivore	1.2	1.4×10^{-2}	0

Organism	Exposure	Endpoint* (mg a.i./kg bw/day)	Food Guild	EDE (mg a.i./kg bw/day)	RQ	Exceedance of LOC
			Fructivore	3.4	3.9×10^{-2}	0
			Herbivore	42.3	4.8×10^{-1}	0

* Acute oral and dietary endpoints that were originally expressed as a concentration (mg a.i./kg diet) have been converted to daily dose (mg a.i./kg bw/day) and further divided by a factor of 10 in order to address differences in species sensitivity.

Table 5 Refined Risk Assessment of Imazamethabenz-Methyl to Terrestrial Plants

Organism	Exposure	EC_{25}	Use Rate (g a.i./ha)	Drift EEC* (g a.i./ha)	RQ	Exceedance of LOC
Plants	Vegetative vigor Black nightshade (*Solanum nigra*)	23 g a.i./ha	500	30	1.3	1.3-fold
			480	28.8	1.3	1.25-fold
			255	15.3	0.7	0
	Transplanted rice** (*Oriza sativa*) emerged plant	146 g a.i./ha	500	30	2.0×10^{-1}	0
			480	28.8	2.0×10^{-1}	0
			255	15.3	1.0×10^{-1}	0

* Based on drift of 6% for a default droplet size of medium (herbicides).

** Transplanted rice is known to grow mainly in aquatic environment, but is treated in risk characterization as a terrestrial plant due to its emerged plant parts.

Table 6 Summary of Screening Level Risk Assessment of Imazamethabenz-Methyl to Aquatic Organisms

Organism	Exposure	Species	Endpoint Reported (mg a.i./L)	Endpoint for RA* (mg a.i./L)	Use Rate (g a.i./ha)	EEC** (mg a.i./L)	RQ	Exceedance of LOC
Freshwater Species								
Invertebrate	Acute	*D. magna*	$LC_{50} > 100$	50	500	0.063	21.3×10^{-3}	0
	Chronic	*D. magna*	NOEC = 8.5	8.5	500	0.063	7.4×10^{-3}	0
Fish	Acute	Bluegill sunfish (*Lepomis macrochirus*)	$LC_{50} > 8.4$	0.84	500	0.063	7.5×10^{-2}	0
	Chronic	Fathead minnow (*Pimephales promelas*)	NOEC < 0.32	0.32	500	0.063	2.0×10^{-1}	0
Algae	–	algae (*Anabaena flos-aquae*)	EC_{50} = 26.9	13.45	500	0.063	4.7×10^{-3}	0
Vascular Plant	Acute	Duckweed (*Lemna gibba*) Immersed plant	EC_{50} = 0.0727	0.0364	500	0.063	1.73	1.73-fold
Amphibian	Chronic	Fathead minnow (*Pimephales promelas*) (surrogate)	NOEC < 0.32	0.32	500	0.333	1	1.0-fold

* Endpoints used in the acute exposure risk assessment (RA) are derived by dividing the EC_{50} or LC_{50} from the appropriate laboratory study by a factor of two (2) for aquatic invertebrates and plants, and by a factor of ten (10) for fish and amphibians.

** EEC based on a 15 cm water body depth for amphibians and a 80 cm water depth for all other aquatic organisms

Table 7 Refined Risk Assessment of Imazamethabenz-Methyl to Aquatic Organisms from Spray Drift

Organism	EC_{50} ÷ 2 or NOEC* (µg a.i./L)	Use Rate (g a.i./ha)	Drift EEC** (µg a.i./L)	RQ	Exceedance of LOC
Plants Duckweed (*Lemna gibba* Immersed plant	36.4	500	3.8	1.0×10^{-1}	0
		480	3.6	9.9×10^{-2}	0
		255	1.92	5.3×10^{-2}	0
Amphibians Fathead minnow (*Pimephales promelas*) (surrogate)	320	500	20	6.3×10^{-2}	0
		480	19.2	6.0×10^{-2}	0
		255	10.2	3.2×10^{-2}	0

* Endpoints used in the acute exposure risk assessment for aquatic plants are derived by dividing the EC_{50} from the appropriate laboratory study by a factor of two (2). NOEC for the surrogate in amphibians is not subjected to safety factor.

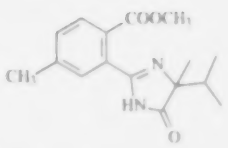
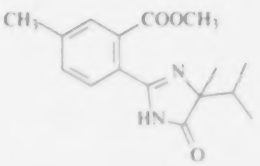
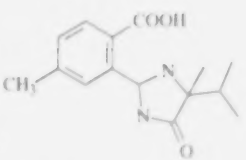
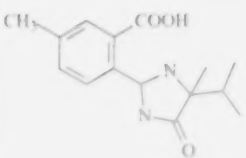
** Based on drift of 6% for a default droplet size of medium (herbicides).

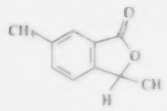
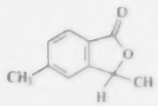
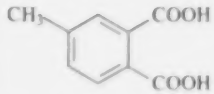
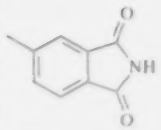
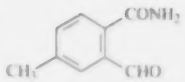
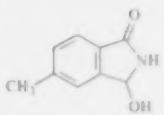
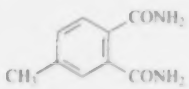
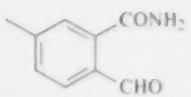
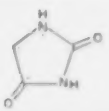
Table 8 Risk Assessment of Imazamethabenz-Methyl for Freshwater Organisms from Predicted Run-off

Endpoint (mg a.i./L)	Use Rate (g a.i./ha)	EEC (mg a.i./L)*	RQ	Exceedance of LOC
Vascular plants				
(EC_{50} ÷ 2) = 0.036	500	0.0253	7.0×10^{-1}	0
Amphibians				
NOEC < 0.32	500	0.0864	2.7×10^{-1}	0

* 90th percentile of 96 hours average runoff for highest values in Canada (Saskatchewan). This time frame was chosen because it most closely matches the 7 day exposure time used to generate the endpoint for the most sensitive aquatic organism, Duckweed (*Lemna gibba*).

Table 9 Imazamethabenz-Methyl and Major Transformation Products

Transformation Product	Company Code	Structure (only provided if formed at >10% in any fate study)	Chemical Process Involved
Para-toluic acid, 2-(4-isopropyl-4-methyl-5-oxo-2-imidazolin-2-yl)-methyl ester	CL 239,589, AC 239,589 or or BAS 512H The para ester of imazamethabenz-methyl (AC 222,293)		Component of the parent ester, imazamethabenz-methyl. No transformation process involved.
Meta-toluic acid, 6-(4-isopropyl-4-methyl-5-oxo-2-imidazolin-2-yl)-methyl ester	CL 252,767, AC 252,767 or BAS 712H The meta ester of imazamethabenz-methyl (AC 222,293)		Component of the parent ester, imazamethabenz-methyl. No transformation process involved.
Mixture of meta-toluic acid, 6-(4-isopropyl-4-methyl-5-oxo-2-imidazolin-2yl) and para-toluic acid, 2-(4-isopropyl-4-methyl-5-oxo-2-imidazolin-2yl) (45:55)	Transformation product CL 263,840 or Reg. No. 4110778 acid (parent acid made of para and meta acid)		Hydrolysis Aerobic soil biotransformation Anaerobic soil biotransformation
Para-toluic acid, 2-(4-isopropyl-4-methyl-5-oxo-2-imidazolin-2-yl)	CL 252,768 (para acid)		Hydrolysis Anaerobic biotransformation
Meta toluic acid, 6-(4-isopropyl-4-methyl-5-oxo-2-imidazolin-2-yl)	CL 222,575 (meta acid)		Hydrolysis Anaerobic soil biotransformation
Toluic acid, 6-[(1-carbamoyl-1,2-dimethylpropy)-caramoyl]- and p-Toluic acid, 2-[(1-carbamoyl-1,2-dimethylpropyl) carbamoyl]	CL 263,068 Amides	 CL 222,575 + CL 252,768	Hydrolysis

Transformation Product	Company Code	Structure (only provided if formed at >10% in any fate study)	Chemical Process Involved
3-hydroxy-6-methyl phthalide	CL 119, 681		From parent ester and parent acid Phototransformation in water
3-hydroxy-5-methyl phthalide	CL 119,682		From Parent ester and parent acid Phototransformation in water
4-methyl phthalic acid	CL 31,025		From parent acid Phototransformation in water
5-methylphthalimide (methylated by gas chromatography)	Unknown		From parent acid Phototransformation in wate
3-hydroxy-5-methyl-phthalimidine	Unknown		From parent acid Phototransformation in water
3-hydroxy-4-methyl-phthalimidine	Unknown		From parent acid Phototransformation in water
4-methyl-phthalamide	Unknown		From parent acid Phototransformation in water
5-methyl, 2-carboxamidebenzaldehyde	Unknown		From parent acid Phototransformation in water
Imidazolidine-2,4-dione	Hydantoin		From parent ester Aerobic soil biotransformation

Appendix IX Monitoring Data

Water Monitoring Data

A search for imazamethabenz-methyl water monitoring data revealed a number of reported detections in surface water in Canada. No monitoring data were available for imazamethabenz-methyl in the United States. No monitoring data were available for imazamethabenz-methyl in groundwater. Most monitoring studies refer to the herbicide as imazamethabenz-methyl-methyl. The use of imazamethabenz-methyl occurs in the Prairie provinces, the Peace River region, the Okanagan Valley and Creston Flats areas of British Columbia. Because several recent reports and water monitoring data for imazamethabenz-methyl were available from the Prairie Region (provincial data as well as data from Environment Canada's Pesticide Science Fund), additional requests for data was not made to the federal, Provincial and Territorial representatives from all of the provinces and territories in Canada. Interestingly, monitoring data from Environment Canada's Pesticide Science Fund were also available for imazamethabenz-methyl in the Ontario Region, where the product is not registered for use. These data were included in the assessments.

Imazamethabenz-methyl was detected in small lakes and in five drinking water reservoirs in Alberta at maximum concentrations of 2.3 and 0.002 µg/L, respectively. In the same province, one surface water site, three streams and five creeks that were known drinking water sources were sampled and had a maximum concentration of 9.0, 1.4 and 0.1 µg/L, respectively. Imazamethabenz-methyl was also detected in small streams in the Niagara area of Ontario at a maximum concentration of 0.009 µg/L, despite the fact that its use is restricted to the Prairie provinces and specific areas in British Columbia.

Imazamethabenz-methyl was also found in water bodies that are unlikely to serve as drinking water source such as the two creeks in Alberta that had a maximum concentration of 12.0 µg/L and many of the northern prairie wetlands that showed a maximum concentration of 0.11 µg/L.

An important limitation of the monitoring data set is that, in many cases, it was not accompanied with use data for imazamethabenz-methyl. For instance, the application rate applied when the application occurred and weather conditions prior to sampling were neither known nor reported. Without this information, it is difficult to conclude if non-detects were a result of non-transport or more simply a result of the inappropriate timing of sampling. In addition, because the data are sparse and concentrations vary in time and space, the maximum concentration reported is unlikely to be the absolute maximum concentration that would be observed in Canada. Factors that may result in higher concentrations being detected includes application done at higher rates, precipitation and some areas and soils being simply more prone to leaching and/or run off. Sampling at intervals immediately following application would increase the likelihood that the maximum concentration would be detected.

Thus, it is likely that imazamethabenz-methyl was not used in some of the areas monitored and that concentrations of imazamethabenz-methyl may be higher in other areas that have not been monitored. The imazamethabenz-methyl monitoring data most likely underestimated the peak exposure because of the following limitations.

- In general, the data are sparse in both time and location. In some of the studies available, imazamethabenz-methyl was analysed in samples that were taken from non-use areas. Imazamethabenz-methyl use information from the areas surrounding where the samples were collected is often not available.

- In some of the studies, sampling was conducted during periods when imazamethabenz-methyl was not applied in Canada (i.e. October through March).

- The concentrations of pesticides in surface water are directly related to the frequency and timing of monitoring in relation to pesticide application and runoff events. Therefore, timing and frequency of sampling are likely to be the most important factor influencing the concentration detected and the frequency of detections. Samples are often taken at arbitrary time intervals (i.e. once a month, once a week) and are unlikely to capture the absolute maximum concentration of imazamethabenz-methyl.

The scarcity of monitoring data in Canada and the lack of such data in the United States do not allow for a clear estimate of the residues of imazamethabenz-methyl in potential drinking water sources, especially groundwater, to be calculated through the statistical analysis of monitoring data. The analysis of imazamethabenz-methyl in Canadian waters has only been recently done due to analytical methodology limitations. The drinking water values currently available for use in the PMRA aggregate dietary risk assessment are those determined by the Level 1 water models.

Appendix X Supplemental Maximum Residue Limit Information—International Situation and Trade Implications

MRLs may vary from one country to another for a number of reasons, including differences in pesticide use patterns and the locations of the field crop trials used to generate residue chemistry data. For animal commodities, differences in MRLs can be due to different livestock feed items and practices.

Table 1 Comparison Between MRLs in Canada and in Other Jurisdictions for Imazamethabenz-Methyl

Raw Agricultural Commodity	Canadian MRL (ppm)	American Tolerance (ppm)
Barley grain	0.1	0.1
Barley straw	-	2
Sunflower seed	0.1	0.1
Wheat grain	0.1	0.1
Wheat straw	-	2

Table 2 Residue Definition in Canada and Other Jurisdictions

Jurisdiction	Residue Definition	
	Plant	Animal
Canada	para and meta isomers of parent methyl ester and acid metabolites	none
United States	para and meta isomers of parent methyl ester and acid metabolites	none

Appendix XI Label Amendments for Commercial Class Products Containing Imazamethabenz-Methyl

Canadian commercial end-use product labels must be amended to include the following statements to further protect workers and the environment.

Label clarifications/revisions

1) For the label for Registration Number 21032, under the DIRECTIONS FOR USE IN ANNUAL RYEGRASS GROWN FOR SEED, the phrase, "PRAIRIE PROVINCES ONLY", must be included in a manner similar to that for DIRECTIONS FOR USE IN SUNFLOWERS.

2) The following statements must be included in the **ENVIRONMENTAL HAZARDS** section.

> TOXIC to aquatic organisms and non-target terrestrial plants. Observe buffer zones specified under **DIRECTIONS FOR USE**.
>
> **Runoff**
> To reduce runoff from treated areas into aquatic habitats avoid application to areas with a moderate to steep slope, compacted soil, or clay.
>
> Avoid application of this product when heavy rain is forecast.
>
> Contamination of aquatic areas as a result of runoff may be reduced by including a vegetative strip between the treated area and the edge of the water body.
>
> **Leaching**
> The use of this chemical may result in contamination of groundwater, particularly in areas where soil pH > 7, are permeable (e.g. sandy soil) and/or the depth to the water table is shallow.

3) The following statements must be included in the **PRECAUTIONS** section.

> Apply only when the potential for drift to areas of human habitation or areas of human activity (houses, cottages, schools and recreational areas) is minimal. Take into consideration wind speed, wind direction, temperature, application equipment and sprayer settings.
>
> Wear a long-sleeved shirt, long pants, shoes plus socks, and chemical-resistant gloves during mixing, loading, application, clean-up and repair. Chemical-resistant gloves are not required while operating groundboom sprayers.

4) The following statements must be included in the **DIRECTIONS FOR USE** section.

Do not re-enter treated fields until 12 hours after application

DO NOT contaminate irrigation or drinking water supplies or aquatic habitats by cleaning of equipment or disposal of wastes.

Field sprayer application: DO NOT apply during periods of dead calm. Avoid application of this product when winds are gusty. DO NOT apply with spray droplets smaller than the American Society of Agricultural Engineers (ASAE) medium classification. Boom height must be 60 cm or less above the crop or ground.

Buffer zones:

The buffer zones specified in the table below are required between the point of direct application and the closest downwind edge of sensitive terrestrial habitats (such as grasslands, forested areas, shelter belts, woodlots, hedgerows, riparian areas and shrublands), sensitive aquatic habitats (such as lakes, rivers, sloughs, ponds, prairie potholes, creeks, marshes, strea, reservoirs, wetlands and estuarine/marine habitats).

Method of Application	Crop	Buffer Zones (metres) Required for the Protection of:		
		Aquatic Habitat of Depths:		Terrestrial Habitat
		Less than 1 m	Greater than 1 m	
Field sprayer	Sunflower	0	0	1
	Annual Ryegrass (for seed)	1	0	1
	Spring wheat, durum wheat and spring barley	1	0	1

When a tank mixture is used, consult the labels of the tank-mix partners and observe the largest (most restrictive) buffer zone of the products involved in the tank mixture.

5) The following statements must be included in the **DISPOSAL** section.

Disposal statements should be in compliance with the Regulatory Directive DIR99-04, *Disposal Statements for Control Product Labels*.

The label amendments presented above do not include all label requirements for individual end-use products, such as first aid statements, disposal statements, precautionary statements and supplementary protective equipment. Additional information on labels of currently registered products should not be removed unless it contradicts the above label statements.

A submission to request label revisions will be required within 90 days after the re-evaluation decision is finalized.

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